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☐	L3	L2 and crystal	2
☐	L2	AKT3	28
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☐	L1	AKT3	11

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Search Results - Record(s) 1 through 28 of 28 returned.

☐ 1. Document ID: US 6960584 B2

Using default format because multiple data bases are involved.

L2: Entry 1 of 28 File: USPT Nov 1, 2005

US-PAT-NO: 6960584
DOCUMENT-IDENTIFIER: US 6960584 B2

TITLE: Inhibitors of Akt activity

DATE-ISSUED: November 1, 2005

INVENTOR-INFORMATION:

NAME	CITY	STATE	ZIP CODE	COUNTRY
Carling; William Robert	Bishop Stortford			GB
Castro Pineiro; Jose Luis	Bishop Stortford			GB
Moore; Kevin William	Buntingford			GB

US-CL-CURRENT: 514/247; 544/236

Full | Title | Citation | Front | Review | Classification | Date | Reference | Sequences | Attachments | Claims | KWIC | Draw D

☐ 2. Document ID: US 6958334 B2

L2: Entry 2 of 28 File: USPT Oct 25, 2005

US-PAT-NO: 6958334
DOCUMENT-IDENTIFIER: US 6958334 B2

TITLE: Inhibitors of Akt activity

DATE-ISSUED: October 25, 2005

INVENTOR-INFORMATION:

NAME	CITY	STATE	ZIP CODE	COUNTRY
Owens; Andrew Pate	Huntingdon			GB
Barnett; Stanley F.	North Wales	PA		

US-CL-CURRENT: 514/248; 544/234

ABSTRACT:

The present invention is directed to compounds comprising a triazolo[4,3-b] pyridazine moiety which inhibit the activity of Akt, a serine/threonine protein kinase. The invention is further directed to chemotherapeutic compositions containing the compounds of this invention and methods for treating cancer comprising administration of the compounds of the invention ##STR1##

6 Claims, 0 Drawing figures
Exemplary Claim Number: 1

Full | Title | Citation | Front | Review | Classification | Date | Reference | Sequences | Attachments | Claims | KWIC | Draw D

☐ 3. Document ID: US 6936450 B2

L2: Entry 3 of 28 File: USPT Aug 30, 2005

US-PAT-NO: 6936450
DOCUMENT-IDENTIFIER: US 6936450 B2

TITLE: Variants of protein kinases

DATE-ISSUED: August 30, 2005

INVENTOR-INFORMATION:

NAME	CITY	STATE	ZIP CODE	COUNTRY
Levine; Zurit	Herzliya			IL
Bernstein; Jeanne	Kfar Yona			IL

US-CL-CURRENT: 435/194; 424/94.6, 530/350

ABSTRACT:

The present invention concerns nucleic acid sequences and amino acid sequences of dominant negative variants of kinases, i.e. of sequences which inhibit activity of kinases in a dominant manner. The invention also concerns pharmaceutical compositions and detection methods using these sequences.

3 Claims, 91 Drawing figures
Exemplary Claim Number: 1
Number of Drawing Sheets: 136

Full | Title | Citation | Front | Review | Classification | Date | Reference | Sequences | Attachments | Claims | KWIC | Draw D

☐ 4. Document ID: US 6905827 B2

L2: Entry 4 of 28 File: USPT Jun 14, 2005

US-PAT-NO: 6905827
DOCUMENT-IDENTIFIER: US 6905827 B2

TITLE: Methods and compositions for diagnosing or monitoring auto immune and

chronic inflammatory diseases

DATE-ISSUED: June 14, 2005

INVENTOR-INFORMATION:

NAME	CITY	STATE	ZIP CODE	COUNTRY
Wohlgemuth; Jay	Palo Alto	CA		
Fry; Kirk	Palo Alto	CA		
Woodward; Robert	Pleasanton	CA		
Ly; Ngoc	San Bruno	CA		

US-CL-CURRENT: 435/6; 435/7.1, 435/91.2

ABSTRACT:

Methods of diagnosing or monitoring an autoimmune or chronic inflammatory disease, particularly SLE in a patient by detecting the expression level of one or more genes or surrogates derived therefrom in the patient are described. Diagnostic oligonucleotides for diagnosing or monitoring chronic inflammatory disease, particularly SLE infection and kits or systems containing the same are also described.

9 Claims, 12 Drawing figures
Exemplary Claim Number: 1
Number of Drawing Sheets: 9

☐ 5. Document ID: US 6881555 B2

L2: Entry 5 of 28 File: USPT Apr 19, 2005

US-PAT-NO: 6881555
DOCUMENT-IDENTIFIER: US 6881555 B2

TITLE: AKT nucleic acids, polypeptides, and uses thereof

DATE-ISSUED: April 19, 2005

INVENTOR-INFORMATION:

NAME	CITY	STATE	ZIP CODE	COUNTRY
Guo; Kun	Eagleville	PA		
Pagnoni; Marco F.	Norristown	PA		
Clark; Kenneth L.	Gilbertsville	PA		
Ivashchenko; Yuri D.	Norristown	PA		

US-CL-CURRENT: 435/69.1; 435/174, 435/176, 435/177, 435/182, 435/320.1, 530/300, 530/350, 536/18.7, 536/22.1, 536/23.1, 536/23.2, 536/23.5

ABSTRACT:

The present invention relates to human Akt3 proteins and polypeptides. The invention also relates to isolated nucleic acids encoding human Akt3, to vectors containing them and to their therapeutic uses, in particular for gene therapy. Expression of Akt3 inhibits cell death associated with hypoxia, apoptosis or necrosis.

50 Claims, 7 Drawing figures
Exemplary Claim Number: 1
Number of Drawing Sheets: 8

☐ 6. Document ID: US 6831175 B2

L2: Entry 6 of 28 File: USPT Dec 14, 2004

US-PAT-NO: 6831175
DOCUMENT-IDENTIFIER: US 6831175 B2

TITLE: Kinase inhibitors

DATE-ISSUED: December 14, 2004

INVENTOR-INFORMATION:

NAME	CITY	STATE	ZIP CODE	COUNTRY
Li; Qun	Libertyville	IL		
Woods; Keith W.	Libertyville	IL		
Zhu; Gui-Dong	Gurnee	IL		
Fischer; John P.	Longmont	CO		
Gong; Jianchun	Deerfield	IL		
Li; Tongmei	Waukegan	IL		
Gandhi; Virajkumar	Park City	IL		
Thomas; Sheela A.	Libertyville	IL		
Packard; Garrick K.	San Diego	CA		
Song; Xiaohong	Park City	IL		
Abrams; Jason N.	Des Plaines	IL		
Diebold; Robert B.	Waukegan	IL		
Dinges; Jurgen	Grayslake	IL		
Hutchins; Charles W.	Green Oaks	IL		
Stoll; Vincent S.	Libertyville	IL		
Rosenberg; Saul H.	Grayslake	IL		
Giranda; Vincent L.	Gurnee	IL		

US-CL-CURRENT: 546/187; 546/193, 546/194, 546/199, 546/275.7

ABSTRACT:

Compounds having the formula ##STR1##

are useful for inhibiting protein kinases. Also disclosed are compositions which

inhibit protein kinases and methods of inhibiting protein kinases in a patient.

21 Claims, 0 Drawing figures
Exemplary Claim Number: 1

Full | Title | Citation | Front | Review | Classification | Date | Reference | Sequences | Attachments | Claims | KWIC | Draw. D

☐ 7. Document ID: US 6809194 B1

L2: Entry 7 of 28 File: USPT Oct 26, 2004

US-PAT-NO: 6809194
DOCUMENT-IDENTIFIER: US 6809194 B1

TITLE: Akt3 inhibitors

DATE-ISSUED: October 26, 2004

INVENTOR-INFORMATION:

NAME	CITY	STATE	ZIP CODE	COUNTRY
Reinhard; Christoph	Alameda	CA		
Jefferson; Anne B.	Oakland	CA		

US-CL-CURRENT: 536/24.5; 435/325, 435/366, 435/375, 435/6, 435/91.1, 536/24.3, 536/24.31, 536/24.33

ABSTRACT:

Inhibitors of human Akt3, including antisense oligonucleotides, methods, and compositions specific for human Akt3, are provided. Methods of using the compositions for modulating Akt3 expression and for regulating cell growth, particularly tumor cell growth, are also provided.

5 Claims, 6 Drawing figures
Exemplary Claim Number: 1
Number of Drawing Sheets: 6

Full | Title | Citation | Front | Review | Classification | Date | Reference | Sequences | Attachments | Claims | KWIC | Draw. D

☐ 8. Document ID: US 6797859 B2

L2: Entry 8 of 28 File: USPT Sep 28, 2004

US-PAT-NO: 6797859
DOCUMENT-IDENTIFIER: US 6797859 B2

TITLE: Vascular tissue preferred promoters

DATE-ISSUED: September 28, 2004

INVENTOR-INFORMATION:

NAME	CITY	STATE	ZIP CODE	COUNTRY
Abbitt; Shane E.	Ankeny	IA		
Li; Chun Ping	Johnston	IA		
Niu; Xiaomu	Johnston	IA		

US-CL-CURRENT: 800/287; 435/320.1, 435/419, 435/468, 536/24.1, 800/278, 800/279, 800/295, 800/317, 800/320

ABSTRACT:

The present invention provides compositions and methods for regulating expression of heterologous nucleotide sequences in a plant. Compositions include a novel nucleotide sequence for a vascular tissue-preferred promoter for the gene encoding prunasin hydrolase and sequences isolated therefrom. A method for expressing a heterologous nucleotide sequence in a plant using the promoter sequences disclosed herein is provided. The method comprises stably incorporating into the genome of a plant cell a nucleotide sequence operably linked to the vascular tissue-preferred promoter of the present invention and regenerating a stably transformed plant that expresses the nucleotide sequence.

19 Claims, 6 Drawing figures
Exemplary Claim Number: 8
Number of Drawing Sheets: 6

☐ 9. Document ID: US 6743791 B2

L2: Entry 9 of 28 File: USPT Jun 1, 2004

US-PAT-NO: 6743791
DOCUMENT-IDENTIFIER: US 6743791 B2

TITLE: Heterocyclic inhibitors of ERK2 and uses thereof

DATE-ISSUED: June 1, 2004

INVENTOR-INFORMATION:

NAME	CITY	STATE	ZIP CODE	COUNTRY
Cao; Jingrong	Newton	MA		
Green; Jeremy	Burlington	MA		
Hale; Michael	Bedford	MA		
Maltais; Francois	Tewksbury	MA		
Straub; Judy	Cambridge	MA		
Tang; Qing	Cambridge	MA		
Aronov; Alex	Watertown	MA		

US-CL-CURRENT: 514/235.8; 514/266.22, 514/275, 544/122, 544/284, 544/331

ABSTRACT:

Described herein are compounds that are useful as protein kinase inhibitors having the formula: ##STR1##

wherein Z.sup.1 and Z.sup.2 are each independently nitrogen or CH and Ring A, T.sub.m R.sup.1, QR.sup.2, U.sub.n R.sup.3, and Sp are as described in the specification. The compounds are especially useful as inhibitors of ERK2 and for treating diseases in mammals that are alleviated by a protein kinase inhibitor, particularly diseases such as cancer, inflammatory disorders, restenosis, diabetes, and cardiovascular disease.

57 Claims, 0 Drawing figures
Exemplary Claim Number: 1

☐ 10. Document ID: US 6649640 B2

L2: Entry 10 of 28 File: USPT Nov 18, 2003

US-PAT-NO: 6649640
DOCUMENT-IDENTIFIER: US 6649640 B2

TITLE: Isoxazole compositions useful as inhibitors of ERK

DATE-ISSUED: November 18, 2003

INVENTOR-INFORMATION:

NAME	CITY	STATE	ZIP CODE	COUNTRY
Hale; Michael	Bedford	MA		
Janetka; James	Beverly	MA		
Maltais; Francois	Somerville	MA		
Cao; Jingrong	West Newton	MA		

US-CL-CURRENT: 514/378; 548/247

ABSTRACT:

Described herein are compounds that are useful as protein kinase inhibitors, especially inhibitors of ERK, having the formula: ##STR1## where A, B, R.sup.1, R.sup.2, T and Ht are described in the specification. The compounds are useful for treating diseases in mammals that are alleviated by a protein kinase inhibitor, particularly diseases such as cancer, inflammatory disorders, restenosis, and cardiovascular disease.

10 Claims, 0 Drawing figures
Exemplary Claim Number: 1

☐ 11. Document ID: US 6495582 B1

L2: Entry 11 of 28 File: USPT Dec 17, 2002

US-PAT-NO: 6495582
DOCUMENT-IDENTIFIER: US 6495582 B1
** See image for Certificate of Correction **

TITLE: Isoxazole compositions useful as inhibitors of ERK

DATE-ISSUED: December 17, 2002

INVENTOR-INFORMATION:

NAME	CITY	STATE	ZIP CODE	COUNTRY
Hale; Michael	Bedford	MA		
Janetka; James	Beverly	MA		
Maltais; Francois	Tewksbury	MA		
Cao; Jingrong	West Newton	MA		
Mashal; Robert	West Newton	MA		

US-CL-CURRENT: 514/378; 548/247

ABSTRACT:

Described herein are compounds that are useful as protein kinase inhibitors, especially inhibitors of ERK, having the formula: ##STR1##

where A, B, R.sup.1, R.sup.2, T and Ht are described in the specification. The compounds are useful for treating diseases in mammals that are alleviated by a protein kinase inhibitor, particularly diseases such as cancer, inflammatory disorders, restenosis, and cardiovascular disease.

25 Claims, 0 Drawing figures
Exemplary Claim Number: 1

Full | Title | Citation | Front | Review | Classification | Date | Reference | Sequences | Attachments | Claims | KWMC | Draw. De

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☐ 12. Document ID: WO 3091246 A1

L2: Entry 12 of 28 File: EPAB Nov 6, 2003

PUB-NO: WO003091246A1
DOCUMENT-IDENTIFIER: WO 3091246 A1
TITLE: PYRROLE DERIVATIVES AS INHIBITORS OF ERK2 AND USES THEREOF

PUBN-DATE: November 6, 2003

INVENTOR-INFORMATION:

NAME	COUNTRY
HALE, MICHAEL R	US
MALTAIS, FRANCOIS	US

TANG, QING	US
STRAUB, JUDITH	US
ARONOV, ALEXANDER	US

INT-CL (IPC): C07 D 403/04; C07 D 401/14; C07 D 403/14; C07 D 405/14; C07 D 487/04; A61 K 31/506; A61 P 35/00
EUR-CL (EPC): C07D401/14; C07D403/04, C07D405/14 , C07D405/14 , C07D471/04

ABSTRACT:

CHG DATE=20031203 STATUS=O>Described herein are compounds that are useful as protein kinase inhibitors having the formula: wherein A1, A2, TmR1, X, R2, R3, R9, R12, and R13 Are as described in the specification. The compounds are especially useful as inhibitors of ERK2, Aurora2, GSK3, CDK2, AKT3, and ROCK protein kinases and for treating diseases in mammals that are alleviated by a protein kinase inhibitor, particularly diseases such as cancer, neurodegenerative disorders, inflammatory disorders, restenosis, diabetes, and cardiovascular disease.

Full | Title | Citation | Front | Review | Classification | Date | Reference | Sequences | Attachments | Claims | KWIC | Draw. D

☐ 13. Document ID: WO 2006022718 A1

L2: Entry 13 of 28 File: DWPI Mar 2, 2006

DERWENT-ACC-NO: 2006-203936
DERWENT-WEEK: 200621

TITLE: New Akt3 polypeptide crystal, useful for identifying therapeutic compounds for the treatment of Akt3 mediated diseases

INVENTOR: BUSSIERE, D; FANG, E ; MURRAY, J

PRIORITY-DATA: 2004WO-US26569 (August 13, 2004)

PATENT-FAMILY:

PUB-NO	PUB-DATE	LANGUAGE	PAGES	MAIN-IPC
WO 2006022718 A1	March 2, 2006	E	228	C12N009/12

INT-CL (IPC): C12 N 9/12; G01 N 33/483

ABSTRACTED-PUB-NO: WO2006022718A
BASIC-ABSTRACT:

NOVELTY - An Akt3 polypeptide crystal where the crystal is resolvable using X-ray crystallography to obtain X-ray patterns for three-dimensional structural determination of the Akt3 polypeptide, is new.

DETAILED DESCRIPTION - INDEPENDENT CLAIMS are also included for:

(1) a co-crystal of an Akt3 polypeptide complexed to an Akt3 binding compound where the co-crystal is resolvable using X-ray crystallography to obtain X-ray patterns

for three dimensional structural determination of the Akt3 complex;

(2) crystallizing an Akt3 polypeptide;

(3) crystallizing an Akt3 polypeptide complexed to a compound;

(4) evaluating the ability of a compound to associate with an Akt3 polypeptide;

(5) identifying a compound capable of modifying Akt3 activity; and

(6) a computer, for producing a three-dimensional representation of a molecule or molecular complex, comprising:

(i) a machine-readable data storage medium comprising a data storage material encoded with machine-readable data, where the data comprises at least a portion of the atomic coordinates given in the specification,

(ii) a working memory for storing instructions for processing the machine-readable data,

(iii) a central-processing unit coupled to the working memory and to the machine-readable data storage medium for processing the machine readable data into the three-dimensional representation, and

(iv) a means for displaying the three-dimensional representation; or a computer, for determining at least a portion of the atomic coordinates corresponding to an X-ray diffraction pattern of a molecule or molecular complex, comprising:

(i) a machine-readable data storage medium comprising a data storage material encoded with machine-readable data, where the data comprises at least a portion of the atomic coordinates given in the specification,

(ii) a machine-readable data storage medium comprising a data storage material encoded with machine-readable data, where the data comprises an X-ray diffraction pattern of the molecule or molecular complex,

(iii) a working memory for storing instructions for processing the machine-readable data of (i) and (ii),

(iv) a central-processing unit coupled to the working memory and to the machine-readable data storage medium of (i) and (ii) for performing a Fourier transform of the machine readable data of (i) and for processing the machine readable data of (ii) into structure coordinates, and

(v) a display coupled to the central-processing unit for displaying the structure coordinates of the molecule or molecular complex.

ACTIVITY - Cytostatic.

No biological data given.

MECHANISM OF ACTION - Akt3-inhibitor.

USE - The crystal and method are useful for identifying compounds capable of modifying Akt3 activity (claimed), which may be useful for the treatment of Akt3 mediated diseases, such as cancer.

☐ 14. Document ID: WO 2005120509 A1, US 20060009460 A1

L2: Entry 14 of 28 File: DWPI Dec 22, 2005

DERWENT-ACC-NO: 2006-048036
DERWENT-WEEK: 200614

TITLE: New quinoline and isoquinoline-based compounds for treating a disease e.g. Alzheimer's disease, stroke, diabetes, obesity, inflammation

INVENTOR: DICKSON, J K; HODGE, C N ; WILLIAMS, K P

PRIORITY-DATA: 2004US-577224P (June 4, 2004), 2005US-0145562 (June 3, 2005)

PATENT-FAMILY:

PUB-NO	PUB-DATE	LANGUAGE	PAGES	MAIN-IPC
WO 2005120509 A1	December 22, 2005	E	106	A61K031/496
US 20060009460 A1	January 12, 2006		000	A61K031/501

INT-CL (IPC): A61 K 31/4709; A61 K 31/4725; A61 K 31/496; A61 K 31/501; C07 D 401/10; C07 D 417/00; C07 D 417/14

ABSTRACTED-PUB-NO: WO2005120509A
BASIC-ABSTRACT:

NOVELTY - Quinoline and isoquinoline-based compounds (I) are new.

DETAILED DESCRIPTION - Quinoline and isoquinoline-based compounds of formula (I), their salts, solvates, chelates, non-covalent complexes and/or prodrugs are new.

Ar = optionally substituted (hetero)aryl;

either A = -N- and B=-CH- or A=-CH and B =-N-;

L = NR1 or O;

R1 = (cyclo)alkyl or heterocycloalkyl (all optionally substituted) or H;

X,Y = CH or N;

G = covalent bond or NR6;

R6 = H or optionally substituted alkyl;

R = optionally substituted heterocycloalkyl.

When Ar is phenyl, A is -N-, B is -CH-, L is NR1, R1 is H, X is CH, Y is CH and G is a covalent bond, then R is not 4-methylpiperazin-1-yl.

ACTIVITY - Nootropic; Neuroprotective; Cerebroprotective; Vasotropic; Antidiabetic; Anorectic; Antiinflammatory; Cytostatic; Antirheumatic; Antiarthritic; Antipsoriatic; Gastrointestinal-Gen.; Immunosuppressive; Virucide; CNS-Gen.; Antibacterial; Antiallergic; Antiasthmatic; Antiangiogenic; Cardiovascular-Gen.; Osteopathic; Ophthalmological; Antiulcer; Nephrotropic; Immunomodulator; Dermatological; Antiparkinsonian; Fungicide; Cardiant; Anti-HIV; Muscular-Gen.;

Antiseborrheic.

MECHANISM OF ACTION - Inhibitor of ATP-utilizing enzyme e.g. a human protein kinase. The ability of N-(4-(4-methylpiperazin-1-yl)phenyl)-6-phe- nylquinolin-4-amine (A) was determined using HTS ATP-utilizing enzyme assay and HTS protocol for developing and running HTS screen in a human protein kinase using the Caliper HTS 250 system. (A) Showed exhibited protein kinase inhibitory activity against MAPKAPK2, PRAK and p38- alpha .

USE - In the manufacture of a medicament for treating a disease e.g. Alzheimer's disease, stroke, diabetes, obesity, inflammation, cancer, Crohn's disease, rheumatoid arthritis, psoriasis and inflammatory bowel disease (claimed), autoimmunological, metabolic, infection, inflammatory disease, disease of central nervous system, degenerative neural disease, allergy/asthma, angiogenesis, neovascularization, vasculogenesis, cardiovascular disease, transplant rejection, osteoarthritis, multiple sclerosis, diabetic retinopathy, ulcerative colitis, renal disease, cachexia, septic shock, lupus, diabetes mellitus, myasthenia gravis, dermatitis, eczema, seborrhea, Parkinson's disease, stem cell protection during chemotherapy, leukemia e.g. myeloid leukemia, Kaposi's sarcoma, ocular disease, corneal disease, glaucoma, bacterial infection, viral infection, fungal infection, heart disease.

ADVANTAGE - The compound inhibits at east one ATP-utilizing enzyme e.g. a human protein kinase such as ABL1, AKT1, AKT2, AKT3, AURORA-A, MBX, c-TAK-1, CDK1, CDK1/cyclin B, CDK2/cyclinA, CDK2/cyclin E, CDK5, CHEK1, CHEK2, CHEK2, CK2, CSK, DAPK1, DYRK2, FLT-3, FYN, GSK- alpha , FSK- beta , HCK, INSR, KIT, LCK, LYNA, MAPKAPK2, MAPKAPK3, MSK1, MSK2, NEK2, p38- alpha , p38- beta , p38- delta , p38-gamma , p70S6K1, PAK2, PDGFR- alpha , PAK1, PKA, PRAK, ROCK2, SGK1, SRC, SYK, PIM-1-kinase, PDK-1 and RSK2.

☐ 15. Document ID: WO 2005089443 A2, US 20050267060 A1

L2: Entry 15 of 28 File: DWPI Sep 29, 2005

DERWENT-ACC-NO: 2005-649559
DERWENT-WEEK: 200604

TITLE: Inducing apoptosis in a melanoma tumor cell, by reducing Akt3 activity through contacting a melanoma tumor cell with an agent that reduces Akt3 activity

INVENTOR: KESTER, M; ROBERTSON, G P ; SANDIRASEGARANE, L ; SHARMA, A

PRIORITY-DATA: 2004US-554509P (March 19, 2004), 2005US-0083583 (March 18, 2005)

PATENT-FAMILY:

PUB-NO	PUB-DATE	LANGUAGE	PAGES	MAIN-IPC
WO 2005089443 A2	September 29, 2005	E	149	A61K000/00
US 20050267060 A1	December 1, 2005		000	A61K048/00

INT-CL (IPC): A61 K 0/00; A61 K 48/00; C12 N 15/87; C12 N 15/88

ABSTRACTED-PUB-NO: WO2005089443A

BASIC-ABSTRACT:

NOVELTY - Inducing apoptosis in a melanoma tumor cell comprises reducing Akt3 activity.

DETAILED DESCRIPTION - INDEPENDENT CLAIMS are also included for treating a melanoma tumor in a mammal, and a pharmaceutical composition for treating a melanoma tumor comprising an agent that reduces Akt3 activity and a carrier.

ACTIVITY - Cytostatic.

No biological data given.

MECHANISM OF ACTION - Gene Therapy.

USE - The methods are useful for inducing apoptosis in a melanoma tumor cell and treating a melanoma tumor in a mammal.

☐ 16. Document ID: US 20050187219 A1, WO 2005082908 A1

L2: Entry 16 of 28 File: DWPI Aug 25, 2005

DERWENT-ACC-NO: 2005-616512
DERWENT-WEEK: 200563

TITLE: New pyrazolo(1,5-a)triazine derivatives useful for treating e.g. viral infections, leukemia, cancer and Kaposi's sarcoma

INVENTOR: GUZI, T J; PARUCH, K

PRIORITY-DATA: 2004US-547685P (February 25, 2004), 2005US-0064044 (February 23, 2005)

PATENT-FAMILY:

PUB-NO	PUB-DATE	LANGUAGE	PAGES	MAIN-IPC
US 20050187219 A1	August 25, 2005		045	A61K031/53
WO 2005082908 A1	September 9, 2005	E	000	C07D487/04

INT-CL (IPC): A61 K 31/53; A61 P 35/00; C07 D 487/04

ABSTRACTED-PUB-NO: US20050187219A
BASIC-ABSTRACT:

NOVELTY - Pyrazolo(1,5-a)triazine derivatives (I), their salts, solvates or esters are new.

DETAILED DESCRIPTION - Pyrazolo(1,5-a)triazine derivatives of formula (I), their salts, solvates or esters are new.

R1 = (cyclo)alkyl, (hetero)aryl, heteroarylalkyl, arylalkyl, or cycloalkylalkyl (all optionally substituted with T, (hetero)aryl or heterocyclyl), H or NR6R7;

R2 = (cyclo)alkyl, alkenyl, alkynyl, trifluoromethyl, -OR7, -SR7, hydroxyalkyl, haloalkyl, halo, CN, (hetero)aryl, formyl, nitro, (hetero)aralkylcarbonyl, alkylcarbonyl or -alkylene-N(R8R9);

R8, R9 = H or alkyl;

NR8R9 = a 5-7 membered heterocycle;

R3 = piperidinyl, pyrrolidinyl (both substituted n times by R10), piperazinyl (substituted at 4-position by R5 and at other positions n times by R10), N-containing heterocycle of formula (i), -NR4R5, H, alkyl, (ar)alkylthio, alkylsulfinyl or aralkylsulfinyl;

R4 = (cyclo)alkyl or heterocyclyl (both optionally mono- to tetra-substituted with T, hydroxymethyl, hydroxyethyl or hydroxypropyl);

R6 = H, alkyl or aryl;

R7 = H or alkyl;

R10 = T or hydroxyalkyl;

T = halo, alkyl, trifluoromethyl, OR6, NR6R7, SR6, SO2R6, CN, SO2N(R6R7) or NO2;

R5 = H, alkyl, aryl, heteroaryl, arylalkyl, cycloalkyl, heterocyclyl, acyl or heteroarylalkyl; and

n = 0 - 4.

Provided that

(1) when R2 is 1-4C alkyl and R5 is H, then R4 is other than 1-4C alkyl;

(2) when R2 is halo, CN, formyl, nitro, alkylcarbonyl, (hetero)aralkylcarbonyl or -alkylene-N(R8R9), then R3 is other than H, (ar)alkylthio, (ar)alkylsulfinyl or -NR4R5 and n is other than 0; and

(3) when R2 is (cyclo)alkyl, alkenyl or alkynyl, then R3 is other than NH(methyl), N,N(dimethyl), NH(acetyl) or N(methyl)(acetyl).

INDEPENDENT CLAIMS are included for the following:

(1) treating at least one disease associated with kinase involving administering to mammal, (I) and at least one anti-cancer agent; and

(2) a pharmaceutical composition (c1) comprising (I) and at least one carrier.

ACTIVITY - Cytostatic; Anti-HIV; Virucide; Antiinflammatory; Dermatological; Immunosuppressive; Nephrotropic; Antiarthritic; Antirheumatic; Antipsoriatic; Gastrointestinal-Gen.; Antidiabetic; Neuroprotective; Nootropic; Antiparkinsonian; Antianemic; Cardiant; Cerebroprotective; Antiarrhythmic; Antiarteriosclerotic; CNS-Gen.; Respiratory-Gen.; Osteopathic; Analgesic.

MECHANISM OF ACTION - Protein Kinase (preferably cyclin dependent kinase-1 (CDK1) CDK2, CDK3, CDK4 or CDK5; mitogen activated protein kinase (MAPK/ERK) or glycogen synthase kinase 3(GSK3 beta), checkpoint kinase-1 (CHK-1), CHK-2, Aurora A - C, AKT1, AKT2 or AKT3) inhibitor; Apoptosis modulator. Kinase activity was determined by performing in vitro CDK2 kinase assay (either cyclin A or E dependent) using 5-((8-ethyl-2-((S)-2-(2-hydroxy-ethyl)-piperidin-1-yl)-pyrazolo(1,5-a)(1,- 3,5) triazin-4-ylamino)methyl)-1-methyl-1H-pyridin-2-one (Ia). Recombinant baculoviruses

expressing cyclins A, E and CDK2 are infected into SF9 cells. IC50 value of (Ia) was 0.00048 mu M.

USE - For inhibiting at least one kinase; or treating at least one disease (e.g. cancer of the bladder, breast, colon, kidney, liver, lung, small cell lung cancer, esophagus, gall bladder, ovary, pancreas, stomach, cervix, thyroid, prostate, and skin including squamous cell carcinoma; leukemia, acute lymphocytic leukemia, acute lymphoblastic leukemia, beta -cell lymphoma, T-cell lymphoma, Hodgkins lymphoma, non-Hodgkins lymphoma, hairy cell lymphoma and Burkett's lymphoma; acute and chronic myelogenous leukemia, myelodysplastic syndrome and promyelocytic leukemia; fibrosarcoma, rhabdomyosarcoma; astrocytoma, neuroblastoma, glioma and schwannomas; melanoma, seminoma, teratocarcinoma, osteosarcoma, xenoderoma pigmentosum, keratoctanthoma, thyroid follicular cancer and Kaposi's sarcoma) associated with the kinase (claimed); also for treatment of viral infections (including but not limited to herpevirus, poxvirus, Epstein-Barr virus, Sindbis virus and adenovirus), prevention of AIDS development in HIV-infected individuals, autoimmune diseases (including systemic lupus erythematous, autoimmune mediated glomerulonephritis, rheumatoid arthritis, psoriasis, inflammatory bowel disease, and autoimmune diabetes mellitus), neurodegenerative disorders (including Alzheimer's disease, AIDS-related dementia, Parkinson's disease, amyotrophic lateral sclerosis, retinitis pigmentosa, spinal muscular atrophy and cerebellar degeneration), myelodysplastic syndromes, aplastic anemia, ischemic injury associated with myocardial infarctions, stroke and reperfusion injury, arrhythmia, atherosclerosis, toxin-induced or alcohol related liver diseases, hematological diseases (including chronic anemia and aplastic anemia), degenerative diseases of the musculoskeletal system (including osteoporosis and arthritis) aspirin-sensitive rhinosinusitis, cystic fibrosis, multiple sclerosis, kidney diseases and cancer pain.

ADVANTAGE - The pyrazolo(1,5-a)triazine derivatives are excellent CDK2 inhibitors.

☐ 17. Document ID: EP 1631548 A2, WO 2004096135 A2

L2: Entry 17 of 28 File: DWPI Mar 8, 2006

DERWENT-ACC-NO: 2004-813791
DERWENT-WEEK: 200618

TITLE: New substituted pyridines useful for treating cancer, a non-malignant disease, restenosis, inflammation, allergy/asthma

INVENTOR: DUGGAN, M; HARTNETT, J ; LINDSLEY, C ; WU, Z ; ZHAO, Z ; DUGGAN, M E ; HARTNETT, J C ; LINDSLEY, C W

PRIORITY-DATA: 2003US-465125P (April 24, 2003)

PATENT-FAMILY:

PUB-NO	PUB-DATE	LANGUAGE	PAGES	MAIN-IPC
EP 1631548 A2	March 8, 2006	E	000	C07D213/02
WO 2004096135 A2	November 11, 2004	E	058	A61K000/00

INT-CL (IPC): A61 K 0/00; A61 K 31/44; C07 D 213/02

ABSTRACTED-PUB-NO: WO2004096135A
BASIC-ABSTRACT:

NOVELTY - A substituted pyridine, its salt and their stereoisomers are new.

DETAILED DESCRIPTION - A substituted pyridine of formula (I), its salt and their stereoisomers are new.

a,b,r,s = 0 or 1;

m,p = 0 - 2;

q,n = 0 - 3;

t = 2 - 6;

R1 = T or G (in which the alkyl, aryl, alkenyl, alkynynl, heterocycle or cycloalkyl are optionally substituted by Rz);

T = (C=O)aOb-1-10C alkyl, (C=O)aOb-aryl, 2-10C alkenyl, 2-10C alkynyl, (C=O)aObheterocyclyl, (C=O)aOb-3-8C cycloalkyl, CO2H, halo, CN, OH, Ob-1-6C perfluoroalkyl, Oa(C=O)bNR6R7, S(O)mRa, S(O)2NR6R7, oxo, CHO, O(C=O)Ob-1-10C alkyl, O(C=O)Ob-3-8C cycloalkyl, OC(=O)Obaryl, O(C=O)Ob-heterocycle or Oa-P=O(OH)2;

G = NRc(C=O)NR6R7, NRcS(O)mRa, NO2 or, NRc(C=O)ObRa;

R2 = G, (C=O)aOb-1-10C alkyl, (C=O)aOb-aryl, 2-10C alkenyl, 2-10C alkynyl, (C=O)aOb-heterocyclyl, (C=O)aOb-3-8C cycloalkyl, CO2H, halo, CN, OH, Ob-1-6C perfluoroalkyl, Oa(C=O)bNR6R7, S(O)mRa, S(O)2NR6R7, CHO, O(C=O)Ob-1-10C alkyl, O(C=O)Ob-3-8C cycloalkyl, OC(=O)Obaryl, O(C=O)Ob-heterocycle or Oa-P=O(OH)2 (in which the alkyl, aryl, alkenyl, alkynynl, heterocycle or cycloalkyl are optionally mono- - tri-substituted by Rz);

R3,R4 = H or 1-6C (perfluoro)alkyl;

R3+R4 = -(CH2)t- (in which one of the carbon atoms is optionally replaced by O, S(O)m, -N(Rb)C(O)- or -N(CORa));

R5 = (C=O)aOb-1-10C alkyl, (C=O)aOb-aryl, 2-10C alkenyl, 2-10C alkynyl, (C=O)aObheterocyclyl, (C=O)aOb-3-8C cycloalkyl, CO2H, halo, CN, OH, Ob-1-6C perfluoroalkyl, Oa(C=O)bNR6R7, S(O)mRa, S(O)2NR6R7, oxo, CHO, O(C=O)Ob-1-10C alkyl, O(C=O)Ob-3-8C cycloalkyl, Oa-P=O(OH)2, NRc(C=O)NR6R7, NRcS(O)mRa or NO2 (in which the alkyl, aryl, alkenyl, alkynynl, heterocycle or cycloalkyl are optionally substituted by Rz);

R6,R7 = H, (C=O)ObRa, 1-10C alkyl, aryl, 2-10C alkenyl, 2-10C alkynyl, heterocyclyl, 3-8C cycloalkyl, SO2Ra, (C=O)N(Rb)2, OH or Oa-P=O(OH)2 (in which the alkyl, aryl, alkenyl, alkynynl, heterocycle or cycloalkyl are optionally substituted by Rz);

Ra = 1-6C alkyl, 2-6C alkenyl, 2-6C alkynyl, 3-6C cycloalkyl, aryl, heterocyclyl (all optionally substituted), 1-6C perfluoroalkyl or 2,2,2-trifluoroethyl;

Rb = aryl, benzyl, heterocyclyl (all optionally substituted), H, 1-6C alkyl, 3-6C cycloalkyl, (C=O)O-1-6C alkyl, (C=O)-1-6C alkyl or S(O)2Ra;

Rc = H, 1-10C alkyl, aryl, 2-10C alkenyl, 2-10C alkynyl, heterocyclyl, 3-8C cycloalkyl or 1-6C perfluoroalkyl (in which the alkyl, aryl, alkenyl, alkynynl, heterocycle or cycloalkyl are optionally substituted by Rz);

Rz = (C=O)rOs(1-10C)alkyl, Or(1-3C)perfluoroalkyl, (0-6C)alkylene-S(O)mRa, oxo, OH, halo, CN, (C=O)rOs(2-10C)alkenyl, (C=O)rOs(2-10C)alkynyl, (C=O)rOs(3-6C) cycloalkyl, (C=O)rOs(0-6C)alkylene-aryl, (C=O)rOs(0-6C)alkylene-heterocyclyl, (C=O) rOs(0-6C)alkylene-N(Rb)2, C(O)Ra, (0-6C)alkylene-CO2Ra, C(O)H, (0-6C)alkylene-CO2H, C(O)N(Rb)2, S(O)mRa, S(O)2N(Rb)2, NRc(C=O)ObRa, O(C=O)Ob-1-10C alkyl, O(C=O)Ob-3-8C cycloalkyl, O(C=O)Obaryl, O(C=O)Ob-heterocycle or Oa-P=O(OH)2 (in which the (cyclo) alkyl, alkenyl, alkynyl, aryl or heterocyclyl are optionally mono- - -tri- substituted by Rb, OH, 1-6C alkoxy, halogen, CO2H, CN, O(C=O)-1-6C alkyl, oxo, N (Rb)2 or Oa-P=O(OH)2).

INDEPENDENT CLAIMS are included for the following:

(a) a pharmaceutical composition comprising a carrier in which (I) is dispersed; and

(b) treating cancer involving (I) in combination with radiation therapy.

ACTIVITY - Cytostatic; Anti-HIV; Ophthalmological; Antidiabetic; Antiarteriosclerotic; Vulnerary; Antiarthritic; Antipsoriatic; Anorectic; Neuroprotective; Nootropic; Vasotropic; Antiinflammatory; Immunosuppressive; Antiallergic; Antiasthmatic.

MECHANISM OF ACTION - Inhibitor of isoforms of Serine/threonine protein kinase, Akt; Tumor cell metastasis inhibitor; Inhibitor of growth of blood vessels.

The compounds (I) were tested in PKC assay and were found to be have IC50 value of at most 50 mu M against at least one of Akt1, Akt2 and Akt3. No results for specific compounds are given.

USE - For treating cancer, non-malignant disease, hyperproliferative disease e.g. restenosis, inflammation, autoimmune diseases and allergy/asthma and hyperinsulinism (claimed), kaposi's sarcoma, Hodgkin's disease, keloids, psoriasis, adrenal glands, ocular neovascular diseases, diabetic retinopathy, retinal vascularization, age-related macular degeneration, atherosclerosis, arthritis, obesity, Alzheimer's disease.

ADVANTAGE - The compounds selectively inhibit isoforms of Serine/threonine kinase or Akt.

☐ 18. Document ID: EP 1622616 A2, WO 2004096131 A2

L2: Entry 18 of 28 File: DWPI Feb 8, 2006

DERWENT-ACC-NO: 2004-813790
DERWENT-WEEK: 200611

TITLE: New substituted pyridine derivatives useful for treating e.g. cancer, atherosclerosis, arthritis, psoriasis, obesity and Alzheimer's disease, are inhibitors of protein kinases

INVENTOR: BILODEAU, M; DUGGAN, M ; HARTNETT, J ; LINDSLEY, C ; WU, Z ; ZHAO, Z ; BILODEAU, M T ; DUGGAN, M E ; HARTNETT, J C ; LINDSLEY, C W

PRIORITY-DATA: 2003US-465260P (April 24, 2003)

PATENT-FAMILY:

PUB-NO	PUB-DATE	LANGUAGE	PAGES	MAIN-IPC
EP 1622616 A2	February 8, 2006	E	000	A61K031/445
WO 2004096131 A2	November 11, 2004	E	064	A61K000/00

INT-CL (IPC): A61 K 0/00; A61 K 31/445; C07 D 401/00; C07 D 401/14

ABSTRACTED-PUB-NO: WO2004096131A
BASIC-ABSTRACT:

NOVELTY - Substituted pyridine derivatives (I) are new.

DETAILED DESCRIPTION - Substituted pyridine derivatives of formula (I), their salts and stereoisomers are new.

a,b,r,s = 0 or 1;

m,p = 0 - 2;

n,q = 0 - 3;

t = 2 - 6;

N' = N-containing heterocyclic (attached to C(R3)(R4) via N);

Q = 1-6C alkyl, aryl or heterocyclyl (all optionally substituted by 1-3 Rz), halo or -NR6R7;

R1 = T', G, -N=CHN(Rb)2 or 1-6C alkyl(C=NRb)N(Rb)2 (in which the alkyl, aryl, alkenyl, alkynynl, heterocycle or cycloalkyl are optionally substituted by Rz);

T' = (C=O)aOb-1-10C alkyl, (C=O)aOb-aryl, 2-10C alkenyl, 2-10C alkynyl, (C=O)aObheterocyclyl, (C=O)aOb-3-8C cycloalkyl, CO2H, halo, CN, OH, Ob-1-6C perfluoroalkyl, Oa(C=O)bNR6R7, S(O)mRa, S(O)2NR6R7, oxo, CHO, O(C=O)Ob-1-10C alkyl, O(C=O)Ob-3-8C cycloalkyl, OC(=O)Obaryl, O(C=O)Ob-heterocycle or Oa-P=O(OH)2;

G = NRc(C=O)NR6R7, NRcS(O)mRa, NO2, NRc(C=O)ObRa;

R2 = G, (C=O)aOb-1-10C alkyl, (C=O)aOb-aryl, 2-10C alkenyl, 2-10C alkynyl, (C=O)aObheterocyclyl, (C=O)aOb-3-8C cycloalkyl, CO2H, halo, CN, OH, Ob-1-6C perfluoroalkyl, Oa(C=O)bNR6R7, S(O)mRa, S(O)2NR6R7, CHO, O(C=O)Ob-1-10C alkyl, O(C=O)Ob-3-8C cycloalkyl, OC(=O)Obaryl, O(C=O)Ob-heterocycle or Oa-P=O(OH)2 (in which the alkyl, aryl, alkenyl, alkynynl, heterocycle or cycloalkyl are optionally substituted by 1-3 Rz);

R3,R4 = H or 1-6C (perfluoro)alkyl; or

R3+R4 = -(CH2)t- (in which one of the carbon atoms is optionally replaced by O, S(O)m, -N(Rb)C(O)- or -N(CORa));

R5 = (C=O)aOb-1-10C alkyl, (C=O)aOb-aryl, 2-10C alkenyl, 2-10C alkynyl, (C=O)aObheterocyclyl, (C=O)aOb-3-8C cycloalkyl, CO2H, halo, CN, OH, Ob-1-6C perfluoroalkyl, Oa(C=O)bNR6R7, S(O)mRa, S(O)2NR6R7, oxo, CHO, O(C=O)Ob-1-10C alkyl, O(C=O)Ob-3-8C cycloalkyl, Oa-P=O(OH)2, NRc(C=O)NR6R7, NRcS(O)mRa or NO2 (in which the alkyl, aryl, alkenyl, alkynynl, heterocycle or cycloalkyl are optionally substituted by Rz);

R6,R7 = H, (C=O)ObRa, 1-10C alkyl, aryl, 2-10C alkenyl, 2-10C alkynyl, heterocyclyl, 3-8C cycloalkyl, SO2Ra, (C=O)N(Rb)2, OH or Oa-P=O(OH)2 (in which the

alkyl, aryl, alkenyl, alkynynl, heterocycle or cycloalkyl are optionally substituted by Rz); or

NR6+R7 = monocyclic or bicyclic 4-7-membered heterocycle and optionally containing at least one additional heteroatoms of N, O and S (both optionally substituted by Rz);

Ra = 1-6C alkyl, 2-6C alkenyl, 2-6C alkynyl, 3-6C cycloalkyl, aryl, heterocyclyl (all optionally substituted), 1-6C perfluoroalkyl or 2,2,2-trifluoroethyl;

Rb = aryl, benzyl, heterocyclyl (all optionally substituted), H, 1-6C alkyl, 3-6C cycloalkyl, (C=O)O-1-6C alkyl, (C=O)-1-6C alkyl or S(O)2Ra;

Rc = H, 1-10C alkyl, aryl, 2-10C alkenyl, 2-10C alkynyl, heterocyclyl, 3-8C cycloalkyl or 1-6C perfluoroalkyl (in which the alkyl, aryl, alkenyl, alkynynl, heterocycle or cycloalkyl are optionally substituted by Rz); and

Rz = (C=O)rOs(1-10C)alkyl, Or(1-3C)perfluoroalkyl, (0-6C)alkylene-S(O)mRa, oxo, OH, halo, CN, (C=O)rOs(2-10C)alkenyl, (C=O)rOs(2-10C)alkynyl, (C=O)rOs(3-6C) cycloalkyl, (C=O)rOs(0-6C)alkylene-aryl, (C=O)rOs(0-6C)alkylene-heterocyclyl, (C=O) rOs(0-6C)alkylene-N(Rb)2, C(O)Ra, (0-6C)alkylene-CO2Ra, C(O)H, (0-6C)alkylene-CO2H, C(O)N(Rb)2, S(O)mRa, S(O)2N(Rb)2, NRc(C=O)ObRa, O(C=O)Ob-1-10C alkyl, O(C=O)Ob-3-8C cycloalkyl, O(C=O)Obaryl, O(C=O)Ob-heterocycle or Oa-P=O(OH)2 (in which the (cyclo) alkyl, alkenyl, alkynyl, aryl or heterocyclyl are optionally substituted by 1-3 Rb, OH, 1-6C alkoxy, halogen, CO2H, CN, O(C=O)-1-6C alkyl, oxo, N(Rb)2 or Oa-P=O(OH)2).

INDEPENDENT CLAIMS are included for the following:

(1) a pharmaceutical composition comprising a carrier in which (I) is dispersed; and

(2) treatment of cancer involving administering (I) in combination with a radiation therapy.

ACTIVITY - Cytostatic; Anti-HIV; Ophthalmological; Antidiabetic; Antiarteriosclerotic; Antiarthritic; Antipsoriatic; Anorectic; Neuroprotective; Nootropic; Vasotropic; Antiinflammatory; Immunosuppressive; Antiallergic; Antiasthmatic.

MECHANISM OF ACTION - Inhibitor of isoforms of Serine/threonine protein kinase, Akt; Tumor cell metastasis inhibitor; Inhibitor of growth of blood vessels. The compounds (I) were tested in PKC assay and were found to be have IC50 value of at most 50 mu M against at least one of Akt1, Akt2 and Akt3. No results for specific compounds are given.

USE - For treating cancer (claimed) including Kaposi's sarcoma and Hodgkin's disease; non-malignant disease including ocular diseases (e.g. retinal vascularization, diabetic retinopathy and age-related macular degeneration), atherosclerosis, arthritis, psoriasis, obesity and Alzheimer's disease; hyperproliferative disease (e.g. restenosis, inflammation, autoimmune diseases and allergy/asthma); and hyperinsulinism.

ADVANTAGE - The compounds selectively inhibit one or two of the Akt isoforms. The compounds exhibit a decrease in, in vitro inhibitory activity or no in vitro inhibitory activity against truncated Akt proteins lacking PH domain.

☐ 19. Document ID: EP 1620095 A2, WO 2004096130 A2

L2: Entry 19 of 28 File: DWPI Feb 1, 2006

DERWENT-ACC-NO: 2004-813789
DERWENT-WEEK: 200612

TITLE: New pyrazolo(3,4-b)pyridine derivatives, useful for treating e.g. cancer, restenosis, inflammation, allergies, asthma, autoimmune diseases, hyperinsulinism, psoriasis and diabetic retinopathy, are protein kinase inhibitors

INVENTOR: BILODEAU, M; WU, Z ; BILODEAU, M T

PRIORITY-DATA: 2003US-465123P (April 24, 2003)

PATENT-FAMILY:

PUB-NO	PUB-DATE	LANGUAGE	PAGES	MAIN-IPC
EP 1620095 A2	February 1, 2006	E	000	A61K031/44
WO 2004096130 A2	November 11, 2004	E	062	A61K000/00

INT-CL (IPC): A61 K 0/00; A61 K 31/44; C07 D 471/00; C07 D 471/14; C07 D 471/16

ABSTRACTED-PUB-NO: WO2004096130A
BASIC-ABSTRACT:

NOVELTY - Pyrazolo(3,4-b)pyridine derivatives (I) are new.

DETAILED DESCRIPTION - Pyrazolo(3,4-b)pyridine derivatives of formula (I) and their salts and stereoisomers are new.

a,b,r,s = 0 or 1;

m,p = 0 - 2;

q,n = 0 - 3;

t = 2 - 6;

X, Y', Z' = C, N, S or O (provided that one of them is N, S or O);

Q = aryl or heterocyclyl (both optionally substituted by 1-3 Rz), or -NR6R7;

N' = N-containing heterocyclyl (bonded to C(R3)(R4) via N);

R1 = T' or G (in which the alkyl, aryl, alkenyl, alkynynl, heterocycle or cycloalkyl are optionally substituted by Rz);

T' = H, (C=O)aOb-1-10C alkyl, (C=O)aOb-aryl, 2-10C alkenyl, 2-10C alkynyl, (C=O) aObheterocyclyl, (C=O)aOb-3-8C cycloalkyl, CO2H, halo, CN, OH, Ob-1-6C perfluoroalkyl, Oa(C=O)bNR6R7, S(O)mRa, S(O)2NR6R7, oxo, CHO, O(C=O)Ob-1-10C alkyl, O(C=O)Ob-3-8C cycloalkyl, OC(=O)Obaryl, O(C=O)Ob-heterocycle or Oa-P=O(OH)2;

G = NRc(C=O)NR6R7, NRcS(O)mRa, NO2 or, NRc(C=O)ObRa;

R2 = G, (C=O)aOb-1-10C alkyl, (C=O)aOb-aryl, 2-10C alkenyl, 2-10C alkynyl, (C=O)

aOb-heterocyclyl, (C=O)aOb-3-8C cycloalkyl, CO2H, halo, CN, OH, Ob-1-6C perfluoroalkyl, Oa(C=O)bNR6R7, S(O)mRa, S(O)2NR6R7, CHO, O(C=O)Ob-1-10C alkyl, O(C=O)Ob-3-8C cycloalkyl, OC(=O)Obaryl, O(C=O)Ob-heterocycle or Oa-P=O(OH)2 (in which the alkyl, aryl, alkenyl, alkynynl, heterocycle or cycloalkyl are optionallysubstituted by 1-3 Rz);

R3, R4 = H or 1-6C (perfluoro)alkyl; or

R3+R4 = -(CH2)t- (in which one of the carbon atoms is optionally replaced by O, S(O)m, -N(Rb)C(O)- or -N(CORa));

R5 = H, (C=O)aOb-1-10C alkyl, (C=O)aOb-aryl, 2-10C alkenyl, 2-10C alkynyl, (C=O)aObheterocyclyl, (C=O)aOb-3-8C cycloalkyl, CO2H, halo, CN, OH, Ob-1-6C perfluoroalkyl, Oa(C=O)bNR6R7, S(O)mRa, S(O)2NR6R7, oxo, CHO, O(C=O)Ob-1-10C alkyl, O(C=O)Ob-3-8C cycloalkyl, Oa-P=O(OH)2, NRc(C=O)NR6R7, NRcS(O)mRa or NO2 (in which the alkyl, aryl, alkenyl, alkynynl, heterocycle or cycloalkyl are optionally substituted by Rz);

R6, R7 = H, (C=O)ObRa, 1-10C alkyl, aryl, 2-10C alkenyl, 2-10C alkynyl, heterocyclyl, 3-8C cycloalkyl, SO2Ra, (C=O)N(Rb)2, OH or Oa-P=O(OH)2 (in which the alkyl, aryl, alkenyl, alkynynl, heterocycle or cycloalkyl are optionally substituted by Rz); or

NR6R7 = monocyclic or bicyclic 4-7-membered heterocycle and optionally containing at least one additional heteroatoms of N, O and S (both optionally substituted by Rz);

Ra = 1-6C alkyl, 2-6C alkenyl, 2-6C alkynyl, 3-6C cycloalkyl, aryl, heterocyclyl (all optionally substituted), 1-6C perfluoroalkyl or 2,2,2-trifluoroethyl;

Rb = aryl, benzyl, heterocyclyl (all optionally substituted), H, 1-6C alkyl, 3-6C cycloalkyl, (C=O)O-1-6C alkyl, (C=O)-1-6C alkyl or S(O)2Ra;

Rc = 1-10C alkyl, aryl, 2-10C alkenyl, 2-10C alkynyl, heterocyclyl, 3-8C cycloalkyl or 1-6C perfluoroalkyl (in which the alkyl, aryl, alkenyl, alkynynl, heterocycle or cycloalkyl are optionally substituted by Rz);

Rz = (C=O)rOs(1-10C)alkyl, Or(1-3C)perfluoroalkyl, (0-6C)alkylene-S(O)mRa, oxo, OH, halo, CN, (C=O)rOs(2-10C)alkenyl, (C=O)rOs(2-10C)alkynyl, (C=O)rOs(3-6C) cycloalkyl, (C=O)rOs(0-6C)alkylene-aryl, (C=O)rOs(0-6C)alkylene-heterocyclyl, (C=O)rOs(0-6C)alkylene-N(Rb)2, C(O)Ra, (0-6C)alkylene-CO2Ra, C(O)H, (0-6C)alkylene-CO2H, C(O)N(Rb)2, S(O)mRa, S(O)2N(Rb)2, NRc(C=O)ObRa, O(C=O)Ob-1-10C alkyl, O(C=O)Ob-3-8C cycloalkyl, O(C=O)Obaryl, O(C=O)Ob-heterocycle or Oa-P=O(OH)2 (in which the (cyclo) alkyl, alkenyl, alkynyl, aryl or heterocyclyl are optionally mono- - -tri-substituted by Rb, OH, 1-6C alkoxy, halogen, CO2H, CN, O(C=O)-1-6C alkyl, oxo, N(Rb)2 or Oa-P=O(OH)2); and

--- = optional double bond.

INDEPENDENT CLAIMS are included for the following:

(a) a pharmaceutical composition comprising a carrier in which (I) is dispersed; and

(b) treating cancer involving (I) in combination with radiation therapy.

ACTIVITY - Cytostatic; Anti-HIV; Ophthalmological; Antidiabetic; Antiarteriosclerotic; Vulnerary; Antiarthritic; Antipsoriatic; Anorectic; Neuroprotective; Nootropic; Vasotropic; Antiinflammatory; Immunosuppressive; Antiallergic; Antiasthmatic.

MECHANISM OF ACTION - Inhibitor of isoforms of Serine/threonine protein kinase, Akt; Tumor cell metastasis inhibitor; Inhibitor of growth of blood vessels.

The compounds (I) were tested in PKC assay and were found to be have IC50 value of at most 50 mu M against at least one of Akt1, Akt2 and Akt3. No results for specific compounds are given.

USE - For treating cancer, non-malignant disease, hyperproliferative disease e.g. restenosis, inflammation, autoimmune diseases and allergy/asthma and hyperinsulinism (all claimed), Kaposi's sarcoma, Hodgkin's disease, keloids, psoriasis, adrenal glands, ocular neovascular diseases, diabetic retinopathy, retinal vascularization, diabetic retinopathy, age-related macular degeneration, atherosclerosis, arthritis, obesity, Alzheimer's disease.

ADVANTAGE - The compounds selectively inhibit isoforms of Serine/threonine kinase or Akt.

☐ 20. Document ID: EP 1620411 A2, WO 2004096129 A2

L2: Entry 20 of 28 File: DWPI Feb 1, 2006

DERWENT-ACC-NO: 2004-813788
DERWENT-WEEK: 200612

TITLE: New heterocyclic triazine derivatives useful for treating cancer, a non-malignant disease, restenosis, inflammation, allergy/asthma

INVENTOR: BILODEAU, M; LINDSLEY, C ; ZHAO, Z ; BILODEAU, M T ; LINDSLEY, C W

PRIORITY-DATA: 2003US-465124P (April 24, 2003)

PATENT-FAMILY:

PUB-NO	PUB-DATE	LANGUAGE	PAGES	MAIN-IPC
EP 1620411 A2	February 1, 2006	E	000	C07D253/00
WO 2004096129 A2	November 11, 2004	E	064	A61K000/00

INT-CL (IPC): A61 K 0/00; A61 K 31/53; A61 P 35/00; C07 D 253/00; C07 D 253/06

ABSTRACTED-PUB-NO: WO2004096129A
BASIC-ABSTRACT:

NOVELTY - Heterocyclic triazine derivatives (I), their salts and stereoisomers are new.

DETAILED DESCRIPTION - Heterocyclic triazine derivatives of formula (I), their salts and stereoisomers are new.

W-Y = CR1=N, N=CR1, C(=O)-NR'1 or R'1N-C(=O);

a,b,r,s = 0 or 1;

m,p = 0 - 2;

q = 0 - 3;

t = 2 - 6;

Q = aryl or heterocyclyl (both optionally mono- - tri-substituted by Rz), H or -NR6R7;

R1 = T or G (in which the alkyl, aryl, alkenyl, alkynynl, heterocycle or cycloalkyl are optionally substituted by Rz);

T = H, (C=O)aOb-1-10C alkyl, (C=O)aOb-aryl, 2-10C alkenyl, 2-10C alkynyl, (C=O)aObheterocyclyl, (C=O)aOb-3-8C cycloalkyl, CO2H, halo, CN, OH, Ob-1-6C perfluoroalkyl, Oa(C=O)bNR6R7, S(O)mRa, S(O)2NR6R7, oxo, CHO, O(C=O)Ob-1-10C alkyl, O(C=O)Ob-3-8C cycloalkyl, OC(=O)Obaryl, O(C=O)Ob-heterocycle or Oa-P=O(OH)2;

R'1 = T (in which the alkyl, aryl, alkenyl, alkynynl, heterocycle or cycloalkyl are optionally substituted by Rz);

G = NRc(C=O)NR6R7, NRcS(O)mRa, NO2, NRc(C=O)ObRa;

R2 = G, (C=O)aOb-1-10C alkyl, (C=O)aOb-aryl, 2-10C alkenyl, 2-10C alkynyl, (C=O)aObheterocyclyl, (C=O)aOb-3-8C cycloalkyl, CO2H, halo, CN, OH, Ob-1-6C perfluoroalkyl, Oa(C=O)bNR6R7, S(O)mRa, S(O)2NR6R7, CHO, O(C=O)Ob-1-10C alkyl, O(C=O)Ob-3-8C cycloalkyl, OC(=O)Obaryl, O(C=O)Ob-heterocycle or Oa-P=O(OH)2 (in which the alkyl, aryl, alkenyl, alkynynl, heterocycle or cycloalkyl are optionally mono- - tri-substituted by Rz);

R3,R4 = H or 1-6C (perfluoro)alkyl;

R3+R4 = -(CH2)t- (in which one of the carbon atoms is optionally replaced by O, S(O)m, -N(Rb)C(O)- or -N(CORa));

R5 = H, (C=O)aOb-1-10C alkyl, (C=O)aOb-aryl, 2-10C alkenyl, 2-10C alkynyl, (C=O)aObheterocyclyl, (C=O)aOb-3-8C cycloalkyl, CO2H, halo, CN, OH, Ob-1-6C perfluoroalkyl, Oa(C=O)bNR6R7, S(O)mRa, S(O)2NR6R7, oxo, CHO, O(C=O)Ob-1-10C alkyl, O(C=O)Ob-3-8C cycloalkyl, Oa-P=O(OH)2, NRc(C=O)NR6R7, NRcS(O)mRa or NO2 (in which the alkyl, aryl, alkenyl, alkynynl, heterocycle or cycloalkyl are optionally substituted by Rz);

R6,R7 = H, (C=O)ObRa, 1-10C alkyl, aryl, 2-10C alkenyl, 2-10C alkynyl, heterocyclyl, 3-8C cycloalkyl, SO2Ra, (C=O)N(Rb)2, OH or Oa-P=O(OH)2 (in which the alkyl, aryl, alkenyl, alkynynl, heterocycle or cycloalkyl are optionally substituted by Rz);

NR6+R7 = monocyclic or bicyclic 4- - 7-membered heterocycle and optionally containing at least one additional heteroatoms of N, O and S (both optionally substituted by Rz);

Ra = 1-6C alkyl, 2-6C alkenyl, 2-6C alkynyl, 3-6C cycloalkyl, aryl, heterocyclyl (all optionally substituted), 1-6C perfluoroalkyl or 2,2,2-trifluoroethyl;

Rb = aryl, benzyl, heterocyclyl (all optionally substituted), H, 1-6C alkyl, 3-6C cycloalkyl, (C=O)O-1-6C alkyl, (C=O)-1-6C alkyl or S(O)2Ra;

Rc = H, 1-10C alkyl, aryl, 2-10C alkenyl, 2-10C alkynyl, heterocyclyl, 3-8C cycloalkyl or 1-6C perfluoroalkyl (in which the alkyl, aryl, alkenyl, alkynynl, heterocycle or cycloalkyl are optionally substituted by Rz);

Rz = (C=O)rOs(1-10C)alkyl, Or(1-3C)perfluoroalkyl, (0-6C)alkylene-S(O)mRa, oxo, OH, halo, CN, (C=O)rOs(2-10C)alkenyl, (C=O)rOs(2-10C)alkynyl, (C=O)rOs(3-6C) cycloalkyl, (C=O)rOs(0-6C)alkylene-aryl, (C=O)rOs(0-6C)alkylene-heterocyclyl, (C=O) rOs(0-6C)alkylene-N(Rb)2, C(O)Ra, (0-6C)alkylene-CO2Ra, C(O)H, (0-6C)alkylene-CO2H, C(O)N(Rb)2, S(O)mRa, S(O)2N(Rb)2, NRc(C=O)ObRa, O(C=O)Ob-1-10C alkyl, O(C=O)Ob-3-8C cycloalkyl, O(C=O)Obaryl, O(C=O)Ob-heterocycle or Oa-P=O(OH)2 (in which the (cyclo) alkyl, alkenyl, alkynyl, aryl or heterocyclyl are optionally mono- - -tri- substituted by Rb, OH, 1-6C alkoxy, halogen, CO2H, CN, O(C=O)-1-6C alkyl, oxo, N (Rb)2 or Oa-P=O(OH)2).

INDEPENDENT CLAIMS are included for the following:

(a) composition comprising a carrier in which (I) is dispersed; and

(b) treating cancer involving (I) in combination with radiation therapy.

ACTIVITY - Cytostatic; Anti-HIV; Ophthalmological; Antidiabetic; Antiarteriosclerotic; Vulnerary; Antiarthritic; Antipsoriatic; Anorectic; Neuroprotective; Nootropic; Vasotropic; Antiinflammatory; Immunosuppressive; Antiallergic; Antiasthmatic.

MECHANISM OF ACTION - Inhibitor of isoforms of Serine/threonine protein kinase, Akt; Tumor cell metastasis inhibitor; Inhibitor of growth of blood vessels.

The compounds (I) were tested in PKC assay and were found to be have IC50 value of at most 50 micro M against at least one of Akt1, Akt2 and Akt3. No results for specific compounds are given.

USE - For treating cancer, non-malignant disease, hyperproliferative disease e.g. restenosis, inflammation, autoimmune diseases and allergy/asthma and hyperinsulinism (claimed), kaposi's sarcoma, Hodgkin's disease, keloids, psoriasis, adrenal glands, ocular neovascular diseases, diabetic retinopathy, retinal vascularization, diabetic retinopathy, age-related macular degeneration, atherosclerosis, arthritis, obesity, Alzheimer's disease.

ADVANTAGE - The compounds selectively inhibit one or two of the Akt isoforms.

☐ 21. Document ID: US 6809194 B1

L2: Entry 21 of 28 File: DWPI Oct 26, 2004

DERWENT-ACC-NO: 2004-755774
DERWENT-WEEK: 200474

TITLE: New Akt3 inhibitor, useful for treating cancer, atherosclerosis, psoriasis, autoimmune diseases, and bacterial and viral infections

INVENTOR: JEFFERSON, A B; REINHARD, C

PRIORITY-DATA: 2000US-203543P (May 10, 2000), 2001US-0851670 (May 8, 2001)

PATENT-FAMILY:

PUB-NO	PUB-DATE	LANGUAGE	PAGES	MAIN-IPC

US 6809194 B1 October 26, 2004 023 C07H021/04

INT-CL (IPC): C07 H 21/04; C12 N 15/85; C12 N 15/86; C12 P 19/34; C12 Q 1/68

ABSTRACTED-PUB-NO: US 6809194B
BASIC-ABSTRACT:

NOVELTY - An isolated Akt3 inhibitor, where the inhibitor is an antisense molecule comprising any of the 13 sequences of 22-29 bp (SEQ ID NOS: 2-6, 12-19), and is not longer than 35 nucleotides in length and is capable of inhibiting the expression of human Akt3, is new.

DETAILED DESCRIPTION - INDEPENDENT CLAIMS are also included for:

(1) a composition comprising a therapeutical amount of an Akt3 antisense molecule;

(2) a method of decreasing the expression of Akt3 in a mammalian cell in vitro comprises administering to the cell an Akt3 inhibitor;

(3) an isolated polynucleotide comprising a polynucleotide:

(i) comprising a transcription initiation region, or

(ii) encoding an antisense oligonucleotide at least 8 nucleotides or nucleotide analogues and not longer than 35 nucleotides in length comprising a sequence of SEQ ID NOS: 2-6, 12-19; and

(4) a recombinant vector comprising the isolated polynucleotide.

ACTIVITY - Antiarteriosclerotic; Antibacterial; Anti-HIV; Antiinflammatory; Antipsoriatic; Cytostatic; Hepatotropic; Immunosuppressive; Virucide.

No biological data given.

MECHANISM OF ACTION - Akt3 inhibitor.

USE - The Akt3 inhibitor, composition, method, and polynucleotide are useful for modulating, i.e. inhibiting, the expression of human Akt3 and for regulating cell growth, particularly tumor cell growth. The Akt3 inhibitor is useful for preparing a medicament for modulating cell proliferation. The antisense compositions and methods are useful for treating tumors, cancers, atherosclerosis, psoriasis, autoimmune diseases, bacterial infections and viral infections like HIV infections or hepatitis.

☐ 22. Document ID: US 20060040943 A1, WO 2004007499 A1, AU 2003251010 A1, EP 1523485 A1, JP 2005534681 W

L2: Entry 22 of 28 File: DWPI Feb 23, 2006

DERWENT-ACC-NO: 2004-191127
DERWENT-WEEK: 200615

TITLE: New 1H-pyrimido(5.4-e)(1,2,4)triazine-5,7-dione derivatives are kinase inhibitors useful for treating cell proliferative disorders such as

atherosclerosis, restenosis and cancer

INVENTOR: BAKKER, A C; BUIJNSTERS, P J J ; CONNORS, R W ; FREYNE, E J E ; HO, C Y ; LACRAMPE, J F A ; RICHARDSON, A

PRIORITY-DATA: 2002EP-0077822 (July 15, 2002)

PATENT-FAMILY:

PUB-NO	PUB-DATE	LANGUAGE	PAGES	MAIN-IPC
US 20060040943 A1	February 23, 2006		000	C07D487/00
WO 2004007499 A1	January 22, 2004	E	080	C07D487/04
AU 2003251010 A1	February 2, 2004		000	C07D487/04
EP 1523485 A1	April 20, 2005	E	000	C07D487/04
JP 2005534681 W	November 17, 2005		078	C07D487/04

INT-CL (IPC): A61 K 31/53; A61 K 31/5377; A61 P 35/00; C07 D 487/00; C07 D 487/04; C07 D 239:00; C07 D 253:00; C07 D 487/04; C07 D 487/04; C07 D 253:00; C07 D 239:00

ABSTRACTED-PUB-NO: WO2004007499A
BASIC-ABSTRACT:

NOVELTY - 1H-pyrimido(5.4-e)(1,2,4)triazine-5,7-dione derivatives (I) and their N-oxide forms, pharmaceutically acceptable addition salts and stereochemically isomeric forms are new.

DETAILED DESCRIPTION - 1H-pyrimido(5.4-e)(1,2,4)triazine-5,7-dione derivatives (I) and their N-oxide forms, pharmaceutically acceptable addition salts and stereochemically isomeric forms are new.

m = 0-1;

n = 0-2;

R1 = H, 1-4C alkyl (optionally substituted with phenyl, pyridinyl or morpholinyl), hydroxy(1-4C)alkyl, 1-4C alkyloxycarbonyl, phenyl (optionally substituted with 1-4C alkyl, 1-4C alkyloxycarbonyl, NO2 and/or cyano(1-4C)alkyl), piperidinyl (optionally substituted with 1-4C alkyl, 1-4C alkyloxycarbonyl or phenyl(1-4C)alkyl), phenyl(1-4C)alkyl or 1-4C alkyloxycarbonyl; either

R2, R3 = H, phenyl, 1-4C alkyl (optionally substituted with phenyl or OH); or

CR2R3 = 3-8C cycloalkyl or Het1 (both optionally substituted with 1-3 of 1-4C alkyloxycarbonyl, phenylcarbonyl 1-4C alkylsulfonyl, aminosulfonyl, mono- or di-(1-4C alkyl)aminosulfonyl and C(=NH)NH2);

R4 = halo, OH, hydroxy(1-4C)alkyl or 1-4C alkyloxy;

R5 = formyl, 1-4C alkyl (optionally substituted with OH, halo, Het3, NR6R7 and/or formyl), 1-4C alkyloxy (optionally substituted with Het4, NR8R9 and/or C(=O)-Het4), Het2, NO2, SO2-Het6, aminosulfonyl or SO2-NR12R13;

R6, R7 = H, 1-4C alkyl (optionally substituted with OH, Het5, 1-4C alkyloxycarbonyl and/or 1-4C alkylsulfonyl), Het5, aminosulfonyl, mono- or di-(1-4C alkyl) aminosulfonyl, 1-4C alkylsulfonyl, 1-4C alkyloxycarbonyl, 1-4C alkyloxy1-4C alkyl or methoxy(1-4C)alkyl;

R8, R9 = H, mono- or di(1-4C alkyl)aminosulfonyl or aminosulfonyl;

R12, R13 = H, 1-4C alkyl or 1-4C alkyloxy1-4C alkyl;

Het1 = piperidinyl;

Het2 = piperidinyl or piperazinyl (optionally substituted with 1-3 1-4C alkyloxycarbonyl);

Het3 = morpholinyl, pyrrolidinyl, piperidinyl or piperazinyl (optionally substituted with 1-3 of OH, 1-4C alkyl, 1-4C alkyloxycarbonyl, hydroxy(1-4C)alkyl, aminosulfonyl, mono- or di(1-4C alkyl)aminosulfonyl, NR10R11, imidazolyl, tetrahydropyrimidinyl, NH2, NH2-SO2-O, mono- or di(1-4C alkyl)amino-SO2-O, NH2-SO2-NH, mono- or di(1-4C alkyl)amino SO2-NH, hydroxy(1-4C alkyloxy)1-4C alkyl, 1-4C alkyloxy(1-4C)alkyl or 1-4C alkyloxy);

R10, R11 = H, 1-4C alkyl, 1-4C alkyloxycarbonyl or mono- or di(1-4C alkyl) aminosulfonyl;

Het4 = morpholinyl, piperidinyl or piperazinyl (optionally substituted with 1-3 of 1-4C alkyl (optionally substituted with one or more OH), aminosulfonyl or mono- or di(1-4C alkyl)aminosulfonyl);

Het5 = pyridinyl, pyrrolidinyl or piperidinyl (optionally substituted with 1-3 of 1-4C alkyl, aminosulfonyl, 1-4C alkyloxycarbonyl or mono- or di(1-4C alkyl) aminosulfonyl); and

Het6 = morpholinyl.

An INDEPENDENT CLAIM is also included for the preparation of (I).

ACTIVITY - Cytostatic; Vasotropic; Antiarteriosclerotic.

MECHANISM OF ACTION - Kinase inhibitor.

A human breast adenocarcinoma cell line (MDA-MB 231) was used in a phosphospecific antibody cell enzyme linked immunosorbent assay (PACE ELISA) to assess the inhibitory effect of (I) on AKT3 mediated phosphorylation of mitogen-activated protein kinase. The results showed that the negative logarithm of median inhibitory concentration (pIC50) of N-(3-(5-(1,6-Dimethyl-5,7-dioxo-1,5,6,7-tetrahydro-pyrimido(5,4-e)(1,2,4)- triazin-3-yl)-furan-2-yl)-benzyl)-methanesulfonamide (Ia). was 6.679.

USE - (I) are useful in the manufacture of medicaments for treating cell proliferative disorders such as atherosclerosis, restenosis and cancer (claimed).

ADVANTAGE - (I) display improved water solubility without loss of biological activity as anti-proliferative compounds.

☐ 23. Document ID: IN 200403005 P4, WO 2003091246 A1, US 20040029857 A1, AU 2003237121 A1, EP 1506189 A1, US 20050234059 A1

L2: Entry 23 of 28 File: DWPI Feb 17, 2006

DERWENT-ACC-NO: 2004-081856
DERWENT-WEEK: 200619

TITLE: New pyrrole derivatives useful for the treatment of e.g. cardiovascular disease, cancer, neurological disorder

INVENTOR: ARONOV, A; HALE, M R ; MALTAIS, F ; STRAUB, J ; TANG, Q

PRIORITY-DATA: 2002US-403853P (August 14, 2002), 2002US-376259P (April 26, 2002), 2003US-0424280 (April 25, 2003), 2005US-0077188 (March 10, 2005)

PATENT-FAMILY:

PUB-NO	PUB-DATE	LANGUAGE	PAGES	MAIN-IPC
IN 200403005 P4	February 17, 2006	E	000	C07D403/04
WO 2003091246 A1	November 6, 2003	E	041	C07D403/04
US 20040029857 A1	February 12, 2004		000	A61K031/541
AU 2003237121 A1	November 10, 2003		000	C07D403/04
EP 1506189 A1	February 16, 2005	E	000	C07D403/04
US 20050234059 A1	October 20, 2005		000	C07D403/04

INT-CL (IPC): A61 K 31/4439; A61 K 31/4545; A61 K 31/496; A61 K 31/501; A61 K 31/506; A61 K 31/53; A61 K 31/5377; A61 K 31/541; A61 P 35/00; C07 D 207:00; C07 D 401/14; C07 D 403/04; C07 D 403/14; C07 D 405/14; C07 D 417/14; C07 D 487/04; C07 D 209:00; C07 D 221:00; C07 D 487/04; C07 D 487/04; C07 D 221:00; C07 D 209:00; C07 D 207:00

ABSTRACTED-PUB-NO: WO2003091246A
BASIC-ABSTRACT:

NOVELTY - Pyrrole derivatives are new.

DETAILED DESCRIPTION - Pyrrole derivatives of formula (I), or their salts are new.

A1 = N or CR10;

A2 = N or CR11;

T = -C(R7)2-, -C(O)-, -C(O)C(O)-, -C(O)NR7-, -C(O)NR7NR7-, -CO2-, -OC(O)-, -NR7CO2-, -O-, -NR7C(O)NR7, -OC(O)NR7-, -NR7NR7-, -NR7C(O)-, -S-, -SO-, -SO2-, -NR7-, -SO2NR7-, -NR7SO2- or -NR7SO2NR7-;

m = 0 or 1;

R1 = Q1;

Q1 = H, CN, halo, R, N(R7)2, OR or OH;

X = -C(O)-, -C(O)NR7, -NR7C(O)-, -NR7SO2-, -SO2NR7-, -S(O)- or -SO2-;

R2 = -(CH2)yR5, -(CH2)yCH(R5)2, -(CH2)yCH(R8)(R5), -(CH2)yCH(R8)CH(R5)2, -N(R4)2, -NR4(CH2)yN(R4)2, -ON(R7)2 or -NR7OR6;

y = 0 - 6;

R3 = -R, -OR6, -SR6, -S(O)R6, -SO2R6, -ON(R7)2, -N(R)2, -NRN(R7)2 or -NROR6;

R6 = H or -R;

R = 3 - 7 membered aromatic monocyclic ring (containing 0 - 3 heteroatoms N, S or O), 8 - 10 membered aromatic bicyclic ring (containing 0 - 4 heteroatoms N, S or O) (both optionally saturated) or 1-6C aliphatic (optionally substituted);

R4 = -R, -R7, -COR7, -CO2R, -CON(R7)2, -SO2R7, -(CH2)yR5 or -(CH2)yCH(R5)2;

R5 = -R, -OR, -CO2R, -(CH2)yN(R7)2, -N(R7)2, -OR7, -SR7, -NR7C(O)R7, -NR7CON(R7)2, -C(O)N(R7)2, -SO2R7, -NR7SO2R7, -C(O)R7, -CN or -SO2N(R7)2;

R7 = H or 1-6C aliphatic (optionally substituted);

NR7+R7 = 3 - 7 membered heterocyclic ring (containing 0 - 2 heteroatoms N, O or S);

R8 = -R, -(CH2)wOR7, -(CH2)wN(R4)2 or -(CH2)wSR7;

w = 0 - 4;

R9 = H, 1-6C aliphatic (optionally substituted), C(O)R7, C(O)OR7 or SO2R7;

R10 = R7, halo, CN, NO2, OR7, SR7, N(R7)2, C(O)R7 or CO2R7;

R10+R3 = optionally substituted 5 - 7 membered aromatic ring (containing 0 - 2 heteroatoms N, O or S);

R11 = R7, CN, NO2, halo, N(R7)2, SR7, OR7, C(O)R7 or CO2R7;

R12 and R13 = R7, CN, NO2, halo, N(R7)2, SR7 or OR7.

Provided that:

(1) when m is 0, then R1 is Q1;

(2) when m is 1, then R1 is H or R;

(3) only one of R12 and R13 is optionally saturated 3 - 7 membered aromatic monocyclic ring (containing 0 - 3 heteroatoms N, S or O) or optionally saturated 8 - 10 membered aromatic bicyclic ring (containing 0 - 4 heteroatoms N, S or O).

INDEPENDENT CLAIMS are included for the following:

(1) a composition (C1) comprises (I), and a carrier, adjuvant or vehicle; and

(2) a composition comprising (I) and a carrier for coating an implantable device.

ACTIVITY - Cardiovascular-Gen.; Vasotropic; Antiarteriosclerotic; Cardiant; Virucide; Neuroprotective; Antibacterial; Immunosuppressive; Antiallergic; Antiinflammatory; Osteopathic; Hepatotropic; Cytostatic; Cerebroprotective; Nootropic; Anti-HIV; Antipsoriatic; Antiparkinsonian; Neuroleptic; CNS-Gen.; Muscular-Gen.; Antirheumatic; Antiarthritic; Antimicrobial; Hypotensive; Antianginal; Antiasthmatic; Ophthalmological; Anticonvulsant.

MECHANISM OF ACTION - Protein kinase inhibitor; Extracellular signal regulated kinase-2 (ERK2) inhibitor; Cyclin-dependent kinase-2 (CDK2) inhibitor; Aurora2 inhibitor; Glycogen synthase kinase-3 (GSK3) inhibitor; AKT3 inhibitor; Rho-associated coiled-coil forming protein serine/threonine kinase (ROCK) inhibitor; Hyperphosphorylated Tau protein inhibitor.

A fixed concentration of activated ERK2 (10 nM) was incubated with various concentrations of 4-(5-methyl-2-phenyl-pyrimidin-4-yl)-1H-pyrrole-2 carboxylic acid

(2-hydroxy-1-(S)-phenyl-ethyl)-amide (A) in dimethylsulfoxide (DMSO) (2.5 %) for 10 minutes at 30 deg. C in 0.1 M HEPES buffer, pH (7.5), containing MgCl2 (10 mM), phosphoenolpyruvate (2.5 mM), NADH (200 micro M), pyruvate kinase (150 micro g/ml), lactate dehydrogenase (50 micro g/ml) and erktide peptide (200 micro M). The reaction was initiated by the addition of ATP (65 micro M). The rate of decrease of absorbance at 340 nM was monitored. (A) showed Ki value of less than 0.1 micro M.

USE - For treating or lessening the severity of proliferative disorders, cardiovascular diseases (e.g. restenosis, cardiomycete hypertrophy, cardiomegaly, atherosclerosis, angina pectoris, hypertension, myocardial infarction and congestive heart failure), viral diseases, neurological disorders, autoimmune disorders, inflammatory disorders, allergic disorders, baldness, immunodeficiency disorder, destructive bone disorder, diabetes and liver disease, cancer (e.g. breast, ovary, cervix, prostate, testis, genitourinary tract, esophagus, larynx, glioblastoma, neuroblastoma, stomach, skin, keratoacanthoma, lung, epidermoid carcinoma, large cell carcinoma, small cell carcinoma, lung adenocarcinoma, bone, colon, adenoma, pancreas, adenocarcinoma, thyroid, follicular carcinoma, undifferentiated carcinoma, papillary carcinoma, seminoma, melanoma, sarcoma, bladder carcinoma, liver carcinoma and biliary passages, kidney carcinoma, myeloid disorders, lymphoid disorders, Hodgkin's, hairy cells, buccal cavity and pharynx (oral), lip, tongue, mouth, pharynx, small intestine, colon-rectum, large intestine, rectum, brain and central nervous system and leukemia), stroke, diabetes, hepatomegaly, Alzheimer's disease, cytomegalovirus, HIV, herpes, psoriasis, Parkinson's disease, multiple sclerosis, schizophrenia, AIDS, AIDS-associated dementia, cystic fibrosis, arteriosclerosis, rheumatoid arthritis, conditions associated with organ transplantation, osteoporosis, infectious diseases, conditions associated with cell death, thrombin-induced platelet aggregation, chronic myelogenous leukemia, pathologic immune condition involving T cell activation, cerebrovascular contraction, asthma, peripheral circulation disorder, premature birth, spasm, retinopathy, CNS disorder, neurodegenerative disease (e.g. amyotrophic lateral sclerosis, Huntington's disease, cerebral ischemia, traumatic injury, glutamate neurotoxicity and hypoxia); and for coating an implantable device (all claimed) (such as prostheses, artificial valves, vascular grafts, stents and catheters).

ADVANTAGE - The compound is capable of binding ERK2, CDK2, Aurora2, GSK3, AKT3 and ROCK protein kinases.

☐ 24. Document ID: US 6881555 B2, WO 200168850 A2, AU 200181466 A

L2: Entry 24 of 28 File: DWPI Apr 19, 2005

DERWENT-ACC-NO: 2001-582452
DERWENT-WEEK: 200527

TITLE: New nucleic acid encoding human Akt3 protein, useful for inhibiting cell death and treating myocardial infarction, ischemia reperfusion injury associated with stroke, liver damage and renal failure

INVENTOR: CLARK, K L; GUO, K ; IVASHCHENKO, Y D ; PAGNONI, M F

PRIORITY-DATA: 2000US-0526043 (March 14, 2000), 1999US-125108P (March 19, 1999)

PATENT-FAMILY:

PUB-NO	PUB-DATE	LANGUAGE	PAGES	MAIN-IPC
US 6881555 B2	April 19, 2005		000	C12P021/06
WO 200168850 A2	September 20, 2001	E	073	C12N015/12
AU 200181466 A	September 24, 2001		000	C12N015/12

INT-CL (IPC): A61 K 48/00; C07 K 14/47; C07 K 16/18; C12 N 11/00; C12 N 11/02; C12 N 11/04; C12 N 11/14; C12 N 15/11; C12 N 15/12; C12 N 15/86; C12 P 21/06; G01 N 33/566

ABSTRACTED-PUB-NO: WO 200168850A
BASIC-ABSTRACT:

NOVELTY - An isolated nucleic acid (I) encoding a human Akt3 protein (AH/PH-domain containing serine/threonine kinase, Akt) comprising a fully defined sequence (S1) of 465 amino acids, its splice variant or allelic variant, where (I) hybridizes under stringent conditions with a nucleic acid containing a nucleotide sequence (S2) of 1570 base pairs defined in the specification, is new.

DETAILED DESCRIPTION - (I) comprises the sequence S2 encoding Akt3 protein of sequence S1 or a polypeptide which specifically binds to an antibody generated against an epitope within a peptide having the sequence (S3) CQQSDCGMLGNWKK or its similar sequence, and it can be amplified by polymerase chain reaction (PCR) using an oligonucleotide primer pair derived from a sequence of 74 base pairs (bp) as given in the specification and TTATTTTTTCCAGGTACCCAGCATGCC.

INDEPENDENT CLAIMS are also included for the following:

(1) an isolated human Akt3 protein (II) comprising S3 or its similar sequence, chosen from a protein encoded by (I), a protein comprising S1, its allelic or splice variant or a protein which specifically binds to an antibody generated against an epitope within a peptide having S3;

(2) a vector (III) comprising (I);

(3) a host cell transfected with (III);

(4) producing (II);

(5) an antigenic peptide (IV) comprising the sequence (S3) or its similar sequence, which is a fragment of (II) and encoded by (I);

(6) an antibody (V) which specifically binds (II);

(7) a pharmaceutical composition comprising (I) in the form of liposomes, a complex with nuclear proteins, lipids or dextran or untreated form, or (III);

(8) inhibiting (VI) Akt3 activity in a cell, by decreasing the level of Akt3 protein in the cell; and

(9) a replication defective recombinant virus comprising (I) in its genome.

ACTIVITY - Cerebroprotective; nootropic; neuroprotective; antiarthritic; osteopathic; vasotropic; hepatotrophic.

MECHANISM OF ACTION - Gene therapy; inhibitor of apoptosis; inhibitor of apoptosis stimulating kinase 1 (ASK1)-induced cell death. Expression of human Akt3 inhibited cell death induced by ASK1. A cytomegalovirus (CMV)- beta -gal plasmid was cotransfected into human embryonic kidney (HEK) 293 cells with the expression

plasmid for ASK1 (pCDNA3-HA-ASK1FL), either alone or in combination with the expression plasmid for Akt3 (CMV6-MyrAkt3HA). Two days after transfection, the cells were stained for beta -galactosidase activity. The results showed that transfection with ASK1 expression plasmid (in the absence of the Akt3 expression plasmid) lead to dramatic decrease in beta -gal positive cells. Cotransfection with the Akt3 expression plasmid significantly inhibited cell death induced by ASK1 as measured by the presence of beta -gal positive cells. These data demonstrated that activated Akt3 prevented cell death induced by ASK1.

USE - (I) operably linked to a regulatory region is useful for inhibiting cell death in cardiac myocytes resulting from hypoxia, apoptosis or necrosis and for treating myocardial infarction or ischemia reperfusion injury, particularly myocardial ischemia reperfusion injury or which is associated with stroke, liver damage, renal failure, organ transplantation or coronary artery bypass grafting. Akt3 protein is useful for screening for molecules, such as agonist or antagonist of Akt3 that stimulate or inhibit Akt3 activity, especially inhibition of apoptosis. The method comprises contacting the protein with a candidate molecule and detecting Akt3 activity i.e. inhibition of apoptosis, by measuring the presence of a marker gene. (III) is useful for increasing Akt3 activity in a cell (claimed). Agonist of Akt3 are useful for improving Akt3 activity during treatment of patients suffering from myocardial infarction or ischemia reperfusion injury and inhibitors of Akt3 activity decrease tumor cell survival and result in tumor regression. Akt3 protects cells from apoptosis. Gene therapy using Akt3 reduces the quantity of cell death and final infarct size, resulting in improved post-infarction function, improved quality of life and reduced mortality. In patients with existing heart failure, gene therapy with Akt3 retards the process of ventricular dilation and slows down disease progression. Akt3 gene therapy is useful for treating other disease states, involving cell death by apoptosis, including Alzheimer's disease, liver degeneration or osteoarthritis.

ADVANTAGE - Gene therapy with Akt3 improves quality of the life, reduces mortality and the need for hospitalization.

☐ 25. Document ID: AU 773450 B2, WO 200077190 A2, AU 200051758 A, BR 200011503 A, EP 1187911 A2, NO 200106025 A, CZ 200104444 A3, KR 2002012270 A, HU 200201663 A2, CN 1360629 A, ZA 200109709 A, MX 2001012748 A1, JP 2003530818 W, NZ 516054 A

L2: Entry 25 of 28 File: DWPI May 27, 2004

DERWENT-ACC-NO: 2001-025336
DERWENT-WEEK: 200465

TITLE: Inducing expression of vascular endothelial growth factor, useful for treating an ischemic condition, e.g. cerebrovascular ischemia, renal ischemia or pulmonary ischemia, comprises administering a serine/threonine protein kinase Akt protein

INVENTOR: CLARK, K; GUO, K ; IVASHCHENKO, Y ; IVASHCHENKO, Y D ; CLARK, K L

PRIORITY-DATA: 1999GB-0026058 (November 3, 1999), 1999US-138724P (June 11, 1999)

PATENT-FAMILY:

PUB-NO	PUB-DATE	LANGUAGE	PAGES	MAIN-IPC

AU 773450 B2	May 27, 2004		000	C12N015/00
WO 200077190 A2	December 21, 2000	E	067	C12N015/00
AU 200051758 A	January 2, 2001		000	
BR 200011503 A	March 5, 2002		000	C12N015/00
EP 1187911 A2	March 20, 2002	E	000	C12N009/12
NO 200106025 A	February 8, 2002		000	C12N000/00
CZ 200104444 A3	May 15, 2002		000	C12N015/00
KR 2002012270 A	February 15, 2002		000	A61K038/45
HU 200201663 A2	August 28, 2002		000	C12N015/00
CN 1360629 A	July 24, 2002		000	C12N009/12
ZA 200109709 A	April 30, 2003		075	C12N000/00
MX 2001012748 A1	July 1, 2003		000	C12N015/00
JP 2003530818 W	October 21, 2003		090	C12N015/09
NZ 516054 A	April 30, 2004		000	C12N015/00

INT-CL (IPC): A61 K 31/7088; A61 K 33/24; A61 K 35/00; A61 K 35/76; A61 K 38/04; A61 K 38/22; A61 K 38/45; A61 K 38/46; A61 K 39/395; A61 K 45/06; A61 K 48/00; A61 P 9/10; C12 N 0/00; C12 N 9/12; C12 N 15/00; C12 N 15/09

ABSTRACTED-PUB-NO: WO 200077190A
BASIC-ABSTRACT:

NOVELTY - A method (M1) of inducing expression of vascular endothelial growth factor (VEGF), particularly in the cells of a patient suffering from an ischemic condition, comprising administering a Serine/threonine protein kinase Akt protein.

DETAILED DESCRIPTION - An INDEPENDENT CLAIM is also included for a method (M2) for inhibiting angiogenesis in a patient suffering from a tumor, comprising inhibiting the level of Akt activity in the patient, therefore inhibiting production of VEGF.

ACTIVITY - Vasotropic; cardiant.

Human skeletal muscle cells (HSKMCs) and human coronary smooth muscle cells (HCASMCs) were infected with recombinant adenoviruses expressing either active mouse Akt1 (AV-mAKT1cak) or constitutively active human Akt3 (AV-hAKT3cak). As a control, cells were infected with an adenovirus expressing green fluorescent protein (AV-GFP). On the day after infection, culture media was collected and the VEGF level was measured by ELISA (Enzyme linked immunoabsorbant assay). Both Av-mAKT1cak and AV-hAKT3cak significantly increased VEGF-165 expression in HSKMCs, while AV-GFP infection had little or no effect. Av-mAKT1cak and AV-hAKT3cak also induced VEGF-165 from HCASMCs.

MECHANISM OF ACTION - Antisense therapy; Akt antagonist; Gene therapy.

USE - The method is useful for treating a patient suffering from an ischemic condition such as cerebrovascular ischemia, renal ischemia, pulmonary ischemia, limb ischemia, myocardial ischemia, or ischemic, idiopathic or hypertrophic cardiomyopathy (claimed).

Full | Title | Citation | Front | Review | Classification | Date | Reference | Sequences | Attachments | Claims | KWIC | Draw D

☐ 26. Document ID: AU 782448 B2, WO 200056866 A2, AU 200038802 A, EP 1144600 A2, NO 200104537 A, BR 200009170 A, KR 2002011972 A, JP 2002539781 W, ZA 200108414

A, US 20030100049 A1, MX 2001009431 A1, US 20050142603 A1

L2: Entry 26 of 28 File: DWPI Jul 28, 2005

DERWENT-ACC-NO: 2000-638260
DERWENT-WEEK: 200553

TITLE: Novel AKT3 nucleic acid and proteins capable of preventing apoptotic cell death induced by apoptosis stimulating kinase 1 useful for treating myocardial infarction or ischemia reperfusion injury

INVENTOR: ASHCHENKO, Y D; CLARK, K L ; GUO, K ; PAGNONI, M F ; IVASHCHENKO, Y D ; PAGNONI, M

PRIORITY-DATA: 1999US-125108P (March 19, 1999), 2000US-0526043 (March 14, 2000), 2005US-0063691 (February 23, 2005)

PATENT-FAMILY:

PUB-NO	PUB-DATE	LANGUAGE	PAGES	MAIN-IPC
AU 782448 B2	July 28, 2005		000	C12N009/12
WO 200056866 A2	September 28, 2000	E	073	C12N009/12
AU 200038802 A	October 9, 2000		000	C12N009/12
EP 1144600 A2	October 17, 2001	E	000	C12N009/12
NO 200104537 A	October 31, 2001		000	C12N000/00
BR 200009170 A	April 30, 2002		000	C12N009/12
KR 2002011972 A	February 9, 2002		000	C12N015/11
JP 2002539781 W	November 26, 2002		098	C12N015/09
ZA 200108414 A	March 26, 2003		098	C12N000/00
US 20030100049 A1	May 29, 2003		000	A61K048/00
MX 2001009431 A1	March 1, 2002		000	A61K038/45
US 20050142603 A1	June 30, 2005		000	C12Q001/68

INT-CL (IPC): A61 K 9/127; A61 K 35/76; A61 K 38/00; A61 K 38/45; A61 K 39/395; A61 K 47/36; A61 K 47/42; A61 K 47/46; A61 K 48/00; A61 P 1/16; A61 P 9/10; A61 P 13/12; A61 P 37/06; A61 P 43/00; C07 H 21/04; C07 K 14/47; C07 K 16/40; C12 N 0/00; C12 N 1/19; C12 N 1/21; C12 N 5/06; C12 N 5/10; C12 N 7/00; C12 N 9/12; C12 N 15/09; C12 N 15/11; C12 N 15/63; C12 P 21/00; C12 P 21/02; C12 Q 1/48; C12 Q 1/68; G01 N 33/15; G01 N 33/50; G01 N 33/53; G01 N 33/566; C12 N 1/19; C12 N 1/21; C12 N 5/10; C12 R 1:01; C12 R 1:645; C12 R 1:91

ABSTRACTED-PUB-NO: WO 200056866A
BASIC-ABSTRACT:

NOVELTY - An isolated nucleic acid (I) encoding a human Akt3 protein, is new.

DETAILED DESCRIPTION - An isolated nucleic acid (I) encoding a human Akt3 protein, is new.

The human Akt3 protein comprises the sequence (S1) CysGlnGlnSerAspCysGlyMe-tLeuGlyAsnTrpLysLys, or a substantially similar sequence. (I) has the following properties:

(a) it can be amplified by polymerase chain reaction (PCR) using an oligonucleotide primer pair derived from a 74 or 27 nucleotide sequence, fully defined in the

specification;

(b) it hybridizes under stringent conditions to a nucleic acid comprising a 1570 base pair sequence, fully defined in the specification;

(c) it encodes a polypeptide comprising a 465 residue amino acid sequence, or its allelic or splice variants; or

(d) it encodes a polypeptide which specifically binds to an antibody generated against an epitope within a peptide having the sequence S1.

INDEPENDENT CLAIMS are also included for the following:

(1) an isolated human Akt3 protein (II) comprising the sequence S1 encoded by (I);

(2) a vector (III) comprising (I);

(3) a host cell (IV) transfected with (III);

(4) preparation of (II), comprising culturing (IV) under expression conditions, and recovering the polypeptide;

(5) an antigenic peptide comprising (II);

(6) an antibody (V) which specifically binds to (II);

(7) a pharmaceutical composition (VI) comprising (I) or (III);

(8) increasing (VII) Akt3 activity in a cell by increasing the level of (II) in the cell;

(9) inhibiting (VIII) Akt3 activity in a cell by decreasing the level of (II) in a cell; and

(10) a replication defective recombinant virus comprising (I) in its genome.

ACTIVITY - Cardiant; Vasotropic; Cerebroprotective; Hepatotropic; Nephrotropic.

MECHANISM OF ACTION - Gene therapy; Inhibitor of cell death induced by apoptotic stimulating kinase 1 (ASK1). The inhibition of ASK1-induced cell death by Akt3 was studied. A cytomegalovirus (CMV)-beta -gal plasmid was cotransfected into human embryonic kidney (HEK)293 cells with the expression plasmid for ASK1 (pCDNA3-HA-ASK1FL), either alone or in combination with the expression plasmid for Akt3 (CMV6-MyrAkt3HA). Two days after transfection, cells were stained for beta -galactosidase activity. Cells were washed with 1x phosphate buffered saline (PBS) and fixed. Fixed cells were stained overnight in a moisture chamber. Transfection with the ASK1 expression plasmid led to decrease in beta -gal positive cells and co-transfection with the Akt3 expression plasmid significantly inhibited cell death induced by ASK1 as measured by the presence of beta -gal positive cells. These data demonstrated that activated Akt3 prevented cell death induced by ASK1.

USE - (I) is useful for inhibiting cell death, preferably in a cardiac myocyte, resulting from hypoxia, apoptosis or necrosis in a patient suffering from myocardial infarction or ischemia reperfusion injury. (I) is useful for treating myocardial infarction or ischemia reperfusion injury, where the reperfusion injury is myocardial ischemia reperfusion injury or is associated with stroke, liver damage, renal failure, organ transplantation or coronary artery by pass grafting, by administering (I) to cardiac myocytes of a patient. (II) is useful for screening agonists and agonists of Akt3 by contacting Akt3 protein with a candidate molecule and detecting Akt3 activity such as inhibition of apoptosis in the presence of the

molecule. Inhibition of apoptosis is measured by the presence of a marker gene. (All claimed).

☐ 27. Document ID: WO 9909845 A1, AU 9886817 A, ZA 9807649 A, US 6235740 B1

L2: Entry 27 of 28 File: DWPI Mar 4, 1999

DERWENT-ACC-NO: 1999-190409
DERWENT-WEEK: 199916

TITLE: New imidazoquinoxaline compounds inhibit protein tyrosine kinases - used to treat e.g. immunological disorders

INVENTOR: BARRISH, J C; CHEN, P ; DAS, J ; IWANOWICZ, E J ; NORRIS, D J ; PADMANABHA, R ; ROBERGE, J Y ; SCHIEVEN, G L

PRIORITY-DATA: 1997US-069159P (December 9, 1997), 1997US-056770P (August 25, 1997), 1998US-0097338 (June 15, 1998)

PATENT-FAMILY:

PUB-NO	PUB-DATE	LANGUAGE	PAGES	MAIN-IPC
WO 9909845 A1	March 4, 1999	E	315	A61K031/54
AU 9886817 A	March 16, 1999		000	C07D403/02
ZA 9807649 A	April 26, 2000		353	C07D000/00
US 6235740 B1	May 22, 2001		000	C07D487/04

INT-CL (IPC): A61 K 31/4745; A61 K 31/495; A61 K 31/54; C07 D 0/00; C07 D 403/02; C07 D 413/14; C07 D 487/04; C07 F 0/00

ABSTRACTED-PUB-NO: US 6235740B
BASIC-ABSTRACT:

NOVELTY - Imidazoquinoxaline compound (I) are new. DETAILED DESCRIPTION - Imidazoquinoxaline compounds (I) and their salts are new: p = 0-4; R1-R3 = H, R6, OH OR6, SH, SR6, C(O)qH, C(O)qR6, OC(O)qR6, SO3H, S(O)qR6, halo, CN, NO2, Z4-NR7R8, Z4-N(R9)-Z5-NR10R11, Z4-N(R12)-Z5-R6, SiR13R14R15, -P(O)(OR6)2, or CH=NOR6; or two R1 groups may together form a carbocycle or heterocycle; q = 1 or 2; R6 = optionally substituted alkyl, alkenyl, alkynyl, cycloalkyl, cycloalkylalkyl, cycloalkenyl, cycloalkenylalkyl, aryl, aralkyl, heterocycle or heterocycloalkyl ; R4, R5 = H, R6 or C(O)R6 or together with the N to which they are attached form a heterocycle; R7-R12 = H or R6; or NR7R8 forms a ring or any two of R9-R11 may together with the N to which they are attached form a ring; R13-R15 = alkyl or phenyl; Z4, Z5 = a bond, -Z11-S(O)q-Z12-, -Z11-C(O)-Z12-, -Z11-C(S)-Z12-, -Z11-(O)-Z12-, -Z11-S-Z12-, -Z11-O- C(O)-Z12- or -Z11-C(O)-O-Z12-; Z11,Z12 = a bond, alkylene, alkenylene or alkynylene; with the proviso that (I) is not 4-amino-7-trifluoromethylimidazo[1,5-a]quinoxaline-3-carb- oxylic acid ethyl ester. The full definitions are given in the DEFINITIONS field. An INDEPENDENT CLAIM is also included for the administration of a compound (I) with one or more of the following: another protein tyrosine kinase inhibitor, cyclosporin A, CTLA4-Ig, antibodies selected from anti-ICAM-3, anti-IL-2-receptor, anti-CD45RB, antiCD2, anti-CD3(OKT-3), anti-CD4, anti-CD80, anti-CD86 and monoclonal antibody AKT3, agents blocking the interaction between CD40 and gp39, fusion proteins constructed

from CD40 and gp39, inhibitors of NF-kappa B function, non-steroidal antiinflammatory drugs, steroids, gold compounds, antiproliferative agents, FK506 (tacrolimus, Prograf), mycophenolate mofetil, cytotoxic drugs, TNF-(-inhibitors, anti-TNF antibodies or soluble TNF receptor and rapamycin (sirolimus or Rapamune) or their derivatives.

USE - (I) are used to treat protein tyrosine kinase associated disorders e.g. transplant (e.g. organ transplant, acute transplant, heterograft or homograft) rejection, protection from ischemic or reperfusion injury e.g. such as that incurred during organ transplant, myocardial infarction, stroke or other causes, transplantation tolerance induction, arthritis e.g. rheumatoid arthritis, psoriatic arthritis or osteoarthritis,multiple sclerosis, inflammatory bowel disease including ulcerative colitis and Crohn's disease, lupus(systemic lupus erythematosis), graft vs. host disease, T-cell mediated hypersensitivity diseases including contact hypersensitivity, delayed-type hypersensitivity and gluten-sensitive enteropathy(Celiac disease), psoriasis, contact dermatitis including that due to poison ivy, Hashimoto's thyroiditis, Sjorgren's syndrome, autoimmune hyperthyroidism such as Grave's disease, Addison's disease (autoimmune disease of the adrenal glands), autoimmune polyglandular disease, autoimmune alopecia, pernicious anemia, vitiligo, autoimmune hypopituatarism, Guillain-Barre syndrome, other autoimmune diseases, cancers where Lck or other Src-family kinases such as Src are activated or overexpressed, such as colon carcinoma and thymoma, or cancers where Src-family kinase activity facilitates tumor growth or survival, glomerulonephritis, serum sickness, uticaria, allergic diseases such as respiratory allergies (asthma, hayfever, allergic rhinitis) or skin allergies, scleracierma, mycosis fungoides, acute inflammatory responses such as acute respiratory distress syndrome and ischemia/reperfusion injury , dermatomyositis, alopecia areata, chronic actinic dermatitis, eczema, Behcet's disease, Pustulosis palmoplanteris, Pyoderma gangrenum, Sezary's syndrome, atopic dermatitis, systemic sclerosis and morphea. ACTIVITY - None given. MECHANISM OF ACTION - protein tyrosine kinase inhibitor ESPECIALLY Src-family kinases such as Lck, Fyn, Lyn, Src, Yes, Hck, Fgr and Blk.
ABSTRACTED-PUB-NO:

WO 9909845A EQUIVALENT-ABSTRACTS:

NOVELTY - Imidazoquinoxaline compound (I) are new. DETAILED DESCRIPTION - Imidazoquinoxaline compounds (I) and their salts are new: p = 0-4; R1-R3 = H, R6, OH OR6, SH, SR6, C(O)qH, C(O)qR6, OC(O)qR6, SO3H, S(O)qR6, halo, CN, NO2, Z4-NR7R8, Z4-N(R9)-Z5-NR10R11, Z4-N(R12)-Z5-R6, SiR13R14R15, -P(O)(OR6)2, or CH=NOR6; or two R1 groups may together form a carbocycle or heterocycle; q = 1 or 2; R6 = optionally substituted alkyl, alkenyl, alkynyl, cycloalkyl, cycloalkylalkyl, cycloalkenyl, cycloalkenylalkyl, aryl, aralkyl, heterocycle or heterocycloalkyl ; R4, R5 = H, R6 or C(O)R6 or together with the N to which they are attached form a heterocycle; R7-R12 = H or R6; or NR7R8 forms a ring or any two of R9-R11 may together with the N to which they are attached form a ring; R13-R15 = alkyl or phenyl; Z4, Z5 = a bond, -Z11-S(O)q-Z12-, -Z11-C(O)-Z12-, -Z11-C(S)-Z12-, -Z11-(O)-Z12-, -Z11-S-Z12-, -Z11-O- C(O)-Z12- or -Z11-C(O)-O-Z12-; Z11,Z12 = a bond, alkylene, alkenylene or alkynylene; with the proviso that (I) is not 4-amino-7-trifluoromethylimidazo[1,5-a]quinoxaline-3-carb- oxylic acid ethyl ester. The full definitions are given in the DEFINITIONS field. An INDEPENDENT CLAIM is also included for the administration of a compound (I) with one or more of the following: another protein tyrosine kinase inhibitor, cyclosporin A, CTLA4-Ig, antibodies selected from anti-ICAM-3, anti-IL-2-receptor, anti-CD45RB, antiCD2, anti-CD3(OKT-3), anti-CD4, anti-CD80, anti-CD86 and monoclonal antibody AKT3, agents blocking the interaction between CD40 and gp39, fusion proteins constructed from CD40 and gp39, inhibitors of NF-kappa B function, non-steroidal antiinflammatory drugs, steroids, gold compounds, antiproliferative agents, FK506 (tacrolimus, Prograf), mycophenolate mofetil, cytotoxic drugs, TNF-(-inhibitors, anti-TNF antibodies or soluble TNF receptor and rapamycin (sirolimus or Rapamune)

or their derivatives.

USE - (I) are used to treat protein tyrosine kinase associated disorders e.g. transplant (e.g. organ transplant, acute transplant, heterograft or homograft) rejection, protection from ischemic or reperfusion injury e.g. such as that incurred during organ transplant, myocardial infarction, stroke or other causes, transplantation tolerance induction, arthritis e.g. rheumatoid arthritis, psoriatic arthritis or osteoarthritis,multiple sclerosis, inflammatory bowel disease including ulcerative colitis and Crohn's disease, lupus(systemic lupus erythematosis), graft vs. host disease, T-cell mediated hypersensitivity diseases including contact hypersensitivity, delayed-type hypersensitivity and gluten-sensitive enteropathy(Celiac disease), psoriasis, contact dermatitis including that due to poison ivy, Hashimoto's thyroiditis, Sjorgren's syndrome, autoimmune hyperthyroidism such as Grave's disease, Addison's disease (autoimmune disease of the adrenal glands), autoimmune polyglandular disease, autoimmune alopecia, pernicious anemia, vitiligo, autoimmune hypopituatarism, Guillain-Barre syndrome, other autoimmune diseases, cancers where Lck or other Src-family kinases such as Src are activated or overexpressed, such as colon carcinoma and thymoma, or cancers where Src-family kinase activity facilitates tumor growth or survival, glomerulonephritis, serum sickness, uticaria, allergic diseases such as respiratory allergies (asthma, hayfever, allergic rhinitis) or skin allergies, scleracierma, mycosis fungoides, acute inflammatory responses such as acute respiratory distress syndrome and ischemia/reperfusion injury , dermatomyositis, alopecia areata, chronic actinic dermatitis, eczema, Behcet's disease, Pustulosis palmoplanteris, Pyoderma gangrenum, Sezary's syndrome, atopic dermatitis, systemic sclerosis and morphea. ACTIVITY - None given. MECHANISM OF ACTION - protein tyrosine kinase inhibitor ESPECIALLY Src-family kinases such as Lck, Fyn, Lyn, Src, Yes, Hck, Fgr and Blk.

Full | Title | Citation | Front | Review | Classification | Date | Reference | Sequences | Attachments | Claims | KWIC | Draw D

☐ 28. Document ID: US 2709676 A

L2: Entry 28 of 28 File: USOC May 31, 1955

US-PAT-NO: 2709676
DOCUMENT-IDENTIFIER: US 2709676 A

TITLE: Production of coke agglomerates

DATE-ISSUED: May 31, 1955

INVENTOR-NAME: KREBS ROBERT W

US-CL-CURRENT: 208/53; 201/42, 201/5, 208/127, 423/DIG.16, 44/572

Full | Title | Citation | Front | Review | Classification | Date | Reference | Sequences | Attachments | Claims | KWIC | Draw D

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Terms	Documents
AKT3	28

Hit List

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Search Results - Record(s) 1 through 19 of 19 returned.

☐ 1. Document ID: US 20060052416 A1

L5: Entry 1 of 19 File: PGPB Mar 9, 2006

PGPUB-DOCUMENT-NUMBER: 20060052416
PGPUB-FILING-TYPE:
DOCUMENT-IDENTIFIER: US 20060052416 A1

TITLE: 2-Amido-thiazole-based compounds exhibiting ATP-utilizing enzyme inhibitory activity, and compositions, and uses thereof

PUBLICATION-DATE: March 9, 2006

INVENTOR-INFORMATION:

NAME	CITY	STATE	COUNTRY
Dickson; John K. JR.	Apex	NC	US
Hodge; Carl Nicholas	Los Gatos	CA	US
Mendoza; Jose Serafin	Chapel Hill	NC	US
Chen; Ke	Chapel Hill	NC	US

US-CL-CURRENT: 514/314; 514/340, 514/370, 546/156, 546/269.7, 548/192

Full | Title | Citation | Front | Review | Classification | Date | Reference | Sequences | Attachments | Claims | KWMC | Draw D

☐ 2. Document ID: US 20060009460 A1

L5: Entry 2 of 19 File: PGPB Jan 12, 2006

PGPUB-DOCUMENT-NUMBER: 20060009460
PGPUB-FILING-TYPE:
DOCUMENT-IDENTIFIER: US 20060009460 A1

TITLE: Quinoline- and isoquinoline-based compounds exhibiting ATP-utilizing enzyme inhibitory activity, and compositions, and uses thereof

PUBLICATION-DATE: January 12, 2006

INVENTOR-INFORMATION:

NAME	CITY	STATE	COUNTRY
Dickson; John K. JR.	Apex	NC	US
Williams; Kevin P.	Chapel Hill	NC	US
Hodge; Carl Nicholas	Los Gatos	CA	US

US-CL-CURRENT: 514/252.02; 514/253.06, 544/238, 544/363

Full | Title | Citation | Front | Review | Classification | Date | Reference | Sequences | Attachments | Claims | KWIC | Draw. D

☐ 3. Document ID: US 20050288347 A1

L5: Entry 3 of 19 File: PGPB Dec 29, 2005

PGPUB-DOCUMENT-NUMBER: 20050288347
PGPUB-FILING-TYPE: new
DOCUMENT-IDENTIFIER: US 20050288347 A1

TITLE: Certain triazole-based compounds, compositions, and uses thereof

PUBLICATION-DATE: December 29, 2005

INVENTOR-INFORMATION:

NAME	CITY	STATE	COUNTRY
Hodge, Carl Nicholas	Los Gatos	CA	US
Dickson, John K. JR.	Apex	NC	US
Popa-Burke, Ioana G.	Durham	NC	US
Mendoza, Jose Serafin	Chapel Hill	NC	US

US-CL-CURRENT: 514/383; 548/263.2, 548/264.8

Full | Title | Citation | Front | Review | Classification | Date | Reference | Sequences | Attachments | Claims | KWIC | Draw. D

☐ 4. Document ID: US 20050203114 A1

L5: Entry 4 of 19 File: PGPB Sep 15, 2005

PGPUB-DOCUMENT-NUMBER: 20050203114
PGPUB-FILING-TYPE: new
DOCUMENT-IDENTIFIER: US 20050203114 A1

TITLE: Kinase inhibitors

PUBLICATION-DATE: September 15, 2005

INVENTOR-INFORMATION:

NAME	CITY	STATE	COUNTRY
Armistead, David M.	Sudbury	MA	US
Bemis, Jean E.	Arlington	MA	US
DiPietro, Lucian V.	Gloucester	MA	US
Geuns-Meyer, Stephanie D.	Medford	MA	US
Habgood, Gregory J.	Merrimac	MA	US
Kim, Joseph L.	Wayland	MA	US
Nunes, Joseph J.	Andover	MA	US
Patel, Vinod F.	Acton	MA	US

Toledo-Sherman, Leticia M.	Venice	CA	US

US-CL-CURRENT: 514/269; 514/275, 544/317, 544/323

Full | Title | Citation | Front | Review | Classification | Date | Reference | Sequences | Attachments | Claims | KWIC | Draw D

☐ 5. Document ID: US 20050187219 A1

L5: Entry 5 of 19 File: PGPB Aug 25, 2005

PGPUB-DOCUMENT-NUMBER: 20050187219
PGPUB-FILING-TYPE: new
DOCUMENT-IDENTIFIER: US 20050187219 A1

TITLE: Pyrazolotriazines as kinase inhibitors

PUBLICATION-DATE: August 25, 2005

INVENTOR-INFORMATION:

NAME	CITY	STATE	COUNTRY
Guzi, Timothy J.	Chatham	NJ	US
Paruch, Kamil	Garwood	NJ	US

US-CL-CURRENT: 514/246; 544/184

Full | Title | Citation | Front | Review | Classification | Date | Reference | Sequences | Attachments | Claims | KWIC | Draw D

☐ 6. Document ID: US 20050131006 A1

L5: Entry 6 of 19 File: PGPB Jun 16, 2005

PGPUB-DOCUMENT-NUMBER: 20050131006
PGPUB-FILING-TYPE: new
DOCUMENT-IDENTIFIER: US 20050131006 A1

TITLE: Receptor tyrosine kinase signaling pathway analysis for diagnosis and therapy

PUBLICATION-DATE: June 16, 2005

INVENTOR-INFORMATION:

NAME	CITY	STATE	COUNTRY
Mukherjee, Ali	Belmont	CA	US
Tang, Mengxiang	San Jose	CA	US
Pannu, Harprit S.	San Jose	CA	US
Chan-Hui, Po-Ying	Mayne Island	CA	GB
Singh, Sharat	Los Altos		US

US-CL-CURRENT: 514/291; 435/6

Full | Title | Citation | Front | Review | Classification | Date | Reference | Sequences | Attachments | Claims | KWIC | Draw De

☐ 7. Document ID: US 20050084905 A1

L5: Entry 7 of 19 File: PGPB Apr 21, 2005

PGPUB-DOCUMENT-NUMBER: 20050084905
PGPUB-FILING-TYPE: new
DOCUMENT-IDENTIFIER: US 20050084905 A1

TITLE: Identification of kinase inhibitors

PUBLICATION-DATE: April 21, 2005

INVENTOR-INFORMATION:

NAME	CITY	STATE	COUNTRY
Prescott, John C.	San Francisco	CA	US
Braisted, Andrew	San Francisco	CA	US
Morrow, Joelle			US

US-CL-CURRENT: 435/7.1; 435/15

Full | Title | Citation | Front | Review | Classification | Date | Reference | Sequences | Attachments | Claims | KWIC | Draw De

☐ 8. Document ID: US 20040249586 A1

L5: Entry 8 of 19 File: PGPB Dec 9, 2004

PGPUB-DOCUMENT-NUMBER: 20040249586
PGPUB-FILING-TYPE: new
DOCUMENT-IDENTIFIER: US 20040249586 A1

TITLE: Molecular modification assays

PUBLICATION-DATE: December 9, 2004

INVENTOR-INFORMATION:

NAME	CITY	STATE	COUNTRY
Boge, Annegret	San Jose	CA	US
Lavis, Luke D.	Madison	WI	US
Sportsman, J. Richard	Palo Alto	CA	US
Hoekstra, Merl F.	Monroe	WA	US
Huang, Wei	Sunnyvale	CA	US

US-CL-CURRENT: 702/57

Full | Title | Citation | Front | Review | Classification | Date | Reference | Sequences | Attachments | Claims | KWIC | Draw De

☐ 9. Document ID: US 20040248884 A1

L5: Entry 9 of 19 File: PGPB Dec 9, 2004

PGPUB-DOCUMENT-NUMBER: 20040248884
PGPUB-FILING-TYPE: new
DOCUMENT-IDENTIFIER: US 20040248884 A1

TITLE: Novel cyclic urea derivatives, preparation thereof and pharmaceutical use thereof as kinase inhibitors

PUBLICATION-DATE: December 9, 2004

INVENTOR-INFORMATION:

NAME	CITY	STATE	COUNTRY
Patek, Marcel	Tucson	AZ	US
Nair, Anil	Tucson	AZ	US
Hittinger, Augustin	Igny	AZ	FR
Nemecek, Conception	Thiais	CO	FR
Bond, Daniel	Tucson	AZ	US
Harlow, Greg	Boulder	NJ	US
Bouchard, Herve	Thiais	AZ	FR
Mauger, Jacques	Tucson	PA	US
Malleron, Jean-Luc	Marcoussis		FR
Palermo, Mark	Peapack		US
Al-Obeidi, Fahad	Tucson		US
Faitg, Thomas	Exton		US
Strobel, Hartmut	Liederbach		DE
Ruf, Sven	Floersheim		DE
Ritter, Kurt	Frankfurt Am Main		DE
El-Ahmad, Youssef	Creteil		FR
Lesuisse, Dominique	Montreuil		FR

US-CL-CURRENT: 514/218; 514/269, 540/575, 544/310

Full | Title | Citation | Front | Review | Classification | Date | Reference | Sequences | Attachments | Claims | KWMC | Draw D

☐ 10. Document ID: US 20040229299 A1

L5: Entry 10 of 19 File: PGPB Nov 18, 2004

PGPUB-DOCUMENT-NUMBER: 20040229299
PGPUB-FILING-TYPE: new
DOCUMENT-IDENTIFIER: US 20040229299 A1

TITLE: Intracellular complexes as biomarkers

PUBLICATION-DATE: November 18, 2004

INVENTOR-INFORMATION:

NAME	CITY	STATE	COUNTRY
Badal, M. Youssouf	Sunnyvale	CA	US
Jin, Xueguang	Santa Clara	CA	US
Salimi-Moosavi, Hossein	Sunnyvale	CA	US
Sharat, Singh	Los Altos	CA	US

US-CL-CURRENT: 435/7.23

Full | Title | Citation | Front | Review | Classification | Date | Reference | Sequences | Attachments | Claims | KWIC | Draw D

☐ 11. Document ID: US 20040143117 A1

L5: Entry 11 of 19 File: PGPB Jul 22, 2004

PGPUB-DOCUMENT-NUMBER: 20040143117
PGPUB-FILING-TYPE: new
DOCUMENT-IDENTIFIER: US 20040143117 A1

TITLE: Inhibitors of akt activity

PUBLICATION-DATE: July 22, 2004

INVENTOR-INFORMATION:

NAME	CITY	STATE	COUNTRY
Barnett, Stanley F.	North Wales	PA	US
Graham, Samuel L.	Schwenksville	PA	US
Remy, David C.	North Wales	PA	US

US-CL-CURRENT: 544/353

Full | Title | Citation | Front | Review | Classification | Date | Reference | Sequences | Attachments | Claims | KWIC | Draw D

☐ 12. Document ID: US 20040116388 A1

L5: Entry 12 of 19 File: PGPB Jun 17, 2004

PGPUB-DOCUMENT-NUMBER: 20040116388
PGPUB-FILING-TYPE: new
DOCUMENT-IDENTIFIER: US 20040116388 A1

TITLE: Kinase inhibitors

PUBLICATION-DATE: June 17, 2004

INVENTOR-INFORMATION:

NAME	CITY	STATE	COUNTRY
Armistead, David M.	Sudbury	MA	US
Bemis, Jean E.	Arlington	MA	US
Buchanan, John L.	Brookline	MA	US

DiPietro, Lucian V.	Gloucester	MA	US
Elbaum, Daniel	Newton	MA	US
Geuns-Meyer, Stephanie D.	Medford	MA	US
Habgood, Gregory J.	Merrimack	MA	US
Kim, Joseph L.	Wayland	MA	US
Marshall, Teresa L.	Stow	MA	US
Novak, Perry M.	Milford	MA	US
Nunes, Joseph J.	Andover	MA	US
Patel, Vinod F.	Acton	MA	US
Toledo-Shrman, Leticia M.	Somerville	MA	US
Zhu, Xiaotian	Watertown	MA	US

US-CL-CURRENT: 514/84; 514/241, 544/205, 544/206

Full | Title | Citation | Front | Review | Classification | Date | Reference | Sequences | Attachments | Claims | KWIC | Draw D

☐ 13. Document ID: US 20040106540 A1

L5: Entry 13 of 19 File: PGPB Jun 3, 2004

PGPUB-DOCUMENT-NUMBER: 20040106540
PGPUB-FILING-TYPE: new
DOCUMENT-IDENTIFIER: US 20040106540 A1

TITLE: Method of treating cancer

PUBLICATION-DATE: June 3, 2004

INVENTOR-INFORMATION:

NAME	CITY	STATE	COUNTRY
Barnett, Stanley F	North Wales	PA	US
DeFeo-Jones, Deborah	Lansdale	PA	US
Haskell, Kathleen M	Colmar	PA	US
Huber, Hans E	Lansdale	PA	US
Nahas, Deborah D	Perkasie	PA	US

US-CL-CURRENT: 514/2

Full | Title | Citation | Front | Review | Classification | Date | Reference | Sequences | Attachments | Claims | KWIC | Draw D

☐ 14. Document ID: US 20040102360 A1

L5: Entry 14 of 19 File: PGPB May 27, 2004

PGPUB-DOCUMENT-NUMBER: 20040102360
PGPUB-FILING-TYPE: new
DOCUMENT-IDENTIFIER: US 20040102360 A1

TITLE: Combination therapy

PUBLICATION-DATE: May 27, 2004

INVENTOR-INFORMATION:

NAME	CITY	STATE	COUNTRY
Barnett, Stanley F.	North Wales	PA	US
DeFeo-Jones, Deborah D.	Lansdale	PA	US
Hartman, George D.	Lansdale	PA	US
Huber, Hans E.	Lansdale	PA	US
Stirdivant, Steven M.	Doylestown	PA	US
Heimbrook, David C.	Coopersburg	PA	US

US-CL-CURRENT: 514/1

Full | Title | Citation | Front | Review | Classification | Date | Reference | Sequences | Attachments | Claims | KWIC | Draw D

☐ 15. Document ID: US 20030232391 A1

L5: Entry 15 of 19 File: PGPB Dec 18, 2003

PGPUB-DOCUMENT-NUMBER: 20030232391
PGPUB-FILING-TYPE: new
DOCUMENT-IDENTIFIER: US 20030232391 A1

TITLE: Identification of kinase inhibitors

PUBLICATION-DATE: December 18, 2003

INVENTOR-INFORMATION:

NAME	CITY	STATE	COUNTRY
Prescott, John C.	San Francisco	CA	US
Braisted, Andrew	San Francisco	CA	US

US-CL-CURRENT: 435/7.1; 435/15

Full | Title | Citation | Front | Review | Classification | Date | Reference | Sequences | Attachments | Claims | KWIC | Draw D

☐ 16. Document ID: US 20030199534 A1

L5: Entry 16 of 19 File: PGPB Oct 23, 2003

PGPUB-DOCUMENT-NUMBER: 20030199534
PGPUB-FILING-TYPE: new
DOCUMENT-IDENTIFIER: US 20030199534 A1

TITLE: Kinase inhibitors

PUBLICATION-DATE: October 23, 2003

INVENTOR-INFORMATION:

NAME	CITY	STATE	COUNTRY

Armistead, David M.	Sudbury	MA	US
Bemis, Jean E.	Arlington	MA	US
DiPietro, Lucian V.	Gloucester	MA	US
Geuns-Meyer, Stephanie D.	Medford	MA	US
Habgood, Gregory J.	Merrimac	MA	US
Kim, Joseph L.	Wayland	MA	US
Nunes, Joseph J.	Andover	MA	US
Patel, Vinod F.	Acton	MA	US
Toledo-Sherman, Leticia M.	Somerville	MA	US

US-CL-CURRENT: 514/275; 544/323, 544/324

Full | Title | Citation | Front | Review | Classification | Date | Reference | Sequences | Attachments | Claims | KWIC | Draw D

☐ 17. Document ID: US 20030144204 A1

L5: Entry 17 of 19 File: PGPB Jul 31, 2003

PGPUB-DOCUMENT-NUMBER: 20030144204
PGPUB-FILING-TYPE: new
DOCUMENT-IDENTIFIER: US 20030144204 A1

TITLE: Akt-based inducible survival switch

PUBLICATION-DATE: July 31, 2003

INVENTOR-INFORMATION:

NAME	CITY	STATE	COUNTRY
Spencer, David	Houston	TX	US

US-CL-CURRENT: 514/12; 435/320.1, 435/325, 514/44, 530/350, 536/23.5

Full | Title | Citation | Front | Review | Classification | Date | Reference | Sequences | Attachments | Claims | KWIC | Draw D

☐ 18. Document ID: US 20030004174 A9

L5: Entry 18 of 19 File: PGPB Jan 2, 2003

PGPUB-DOCUMENT-NUMBER: 20030004174
PGPUB-FILING-TYPE: corrected
DOCUMENT-IDENTIFIER: US 20030004174 A9

TITLE: Kinase inhibitors

PUBLICATION-DATE: January 2, 2003

PRIOR-PUBLICATION:

DOC-ID	DATE
US 0052386 A1	May 2, 2002

INVENTOR-INFORMATION:

NAME	CITY	STATE	COUNTRY
Armistead, David M.	Sudbury	MA	US
Bemis, Jean E.	Arlington	MA	US
DiPietro, Lucian V.	Gloucester	MA	US
Geuns-Meyer, Stephanie D.	Medford	MA	US
Habgood, Gregory J.	Merrimac	MA	US
Kim, Joseph L.	Wayland	MA	US
Nunes, Joseph J.	Andover	MA	US
Patel, Vinod F.	Acton	MA	US
Toledo-Sherman, Leticia M.	Somerville	MA	US

US-CL-CURRENT: 514/269; 514/272, 544/309, 544/323

Full | Title | Citation | Front | Review | Classification | Date | Reference | Sequences | Attachments | Claims | KWIC | Draw D

☐ 19. Document ID: US 20020052386 A1

L5: Entry 19 of 19 File: PGPB May 2, 2002

PGPUB-DOCUMENT-NUMBER: 20020052386
PGPUB-FILING-TYPE: new
DOCUMENT-IDENTIFIER: US 20020052386 A1

TITLE: Kinase inhibitors

PUBLICATION-DATE: May 2, 2002

INVENTOR-INFORMATION:

NAME	CITY	STATE	COUNTRY
Armistead, David M.	Sudbury	MA	US
Bemis, Jean E.	Arlington	MA	US
DiPietro, Lucian V.	Gloucester	MA	US
Geuns-Meyer, Stephanie D.	Medford	MA	US
Habgood, Gregory J.	Merrimac	MA	US
Kim, Joseph L.	Wayland	MA	US
Nunes, Joseph J.	Andover	MA	US
Patel, Vinod F.	Acton	MA	US
Toledo-Sherman, Leticia M.	Somerville	MA	US

US-CL-CURRENT: 514/269; 514/272, 544/309, 544/323

Full | Title | Citation | Front | Review | Classification | Date | Reference | Sequences | Attachments | Claims | KWIC | Draw D

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Search Results - Record(s) 1 through 12 of 12 returned.

☐ 1. Document ID: US 20060069066 A1

L7: Entry 1 of 12 File: PGPB Mar 30, 2006

PGPUB-DOCUMENT-NUMBER: 20060069066
PGPUB-FILING-TYPE:
DOCUMENT-IDENTIFIER: US 20060069066 A1

TITLE: Glycogen synthase kinase-3 inhibitors

PUBLICATION-DATE: March 30, 2006

INVENTOR-INFORMATION:

NAME	CITY	STATE	COUNTRY
Eldar-Finkelman; Hagit	Shoham		IL
Portnoy; Moshe	Givat Shmuel		IL

US-CL-CURRENT: 514/80; 546/22, 548/113

Full | Title | Citation | Front | Review | Classification | Date | Reference | Sequences | Attachments | Claims | KWIC | Draw. D

☐ 2. Document ID: US 20060003431 A1

L7: Entry 2 of 12 File: PGPB Jan 5, 2006

PGPUB-DOCUMENT-NUMBER: 20060003431
PGPUB-FILING-TYPE:
DOCUMENT-IDENTIFIER: US 20060003431 A1

TITLE: Structure of protein kinase C theta

PUBLICATION-DATE: January 5, 2006

INVENTOR-INFORMATION:

NAME	CITY	STATE	COUNTRY
Xu; Zhang Bao	Tewksbury	MA	US
Olland; Stephane	Arlington	MA	US
Wolfrom; Scott	Somerville	MA	US
Malakian; Karl	Boxborough	MA	US
Lin; Laura	Weston	MA	US
Stahl; Mark	Lexington	MA	US
Lee; Julie	Somerville	MA	US

Fitz; Lori	Somerville	MA	US
Greco; Rita	Charlestown	MA	US
Chaudhary; Divya	Andover	MA	US
Somers; William Stuart	Lexington	MA	US
Mosyak; Lidia	Newton	MA	US

US-CL-CURRENT: 435/194; 514/211.08, 702/19

Full | Title | Citation | Front | Review | Classification | Date | Reference | Sequences | Attachments | Claims | KWIC | Draw. D

☐ 3. Document ID: US 20060003322 A1

L7: Entry 3 of 12 File: PGPB Jan 5, 2006

PGPUB-DOCUMENT-NUMBER: 20060003322
PGPUB-FILING-TYPE:
DOCUMENT-IDENTIFIER: US 20060003322 A1

TITLE: Bioinformatically detectable group of novel regulatory genes and uses thereof

PUBLICATION-DATE: January 5, 2006

INVENTOR-INFORMATION:

NAME	CITY	STATE	COUNTRY
Bentwich; Isaac	Kvuzat Shiler		IL

US-CL-CURRENT: 435/6

Full | Title | Citation | Front | Review | Classification | Date | Reference | Sequences | Attachments | Claims | KWIC | Draw. D

☐ 4. Document ID: US 20050142610 A1

L7: Entry 4 of 12 File: PGPB Jun 30, 2005

PGPUB-DOCUMENT-NUMBER: 20050142610
PGPUB-FILING-TYPE: new
DOCUMENT-IDENTIFIER: US 20050142610 A1

TITLE: Variant polypeptides containing plekstrin homology domains and uses therefor

PUBLICATION-DATE: June 30, 2005

INVENTOR-INFORMATION:

NAME	CITY	STATE	COUNTRY
Lambright, David G.	Marlborough	MA	US
Czech, Michael P.	Westborough	MA	US
Cronin, Thomas	Worcester	MA	US

US-CL-CURRENT: 435/7.1; 530/350, 536/23.5

Full | Title | Citation | Front | Review | Classification | Date | Reference | Sequences | Attachments | Claims | KWIC | Draw D

☐ 5. Document ID: US 20050124819 A1

L7: Entry 5 of 12 File: PGPB Jun 9, 2005

PGPUB-DOCUMENT-NUMBER: 20050124819
PGPUB-FILING-TYPE: new
DOCUMENT-IDENTIFIER: US 20050124819 A1

TITLE: Metal-organic polyhedra

PUBLICATION-DATE: June 9, 2005

INVENTOR-INFORMATION:

NAME	CITY	STATE	COUNTRY
Yaghi, Omar M.	Ann Arbor	MI	US
Sudik, Andrea C.	Canton	MI	US

US-CL-CURRENT: 556/148

Full | Title | Citation | Front | Review | Classification | Date | Reference | Sequences | Attachments | Claims | KWIC | Draw D

☐ 6. Document ID: US 20040267510 A1

L7: Entry 6 of 12 File: PGPB Dec 30, 2004

PGPUB-DOCUMENT-NUMBER: 20040267510
PGPUB-FILING-TYPE: new
DOCUMENT-IDENTIFIER: US 20040267510 A1

TITLE: Molecular modeling methods

PUBLICATION-DATE: December 30, 2004

INVENTOR-INFORMATION:

NAME	CITY	STATE	COUNTRY
Bemis, Guy	Arlington	MA	US
Caron, Paul	Malden	MA	US
Hare, Brian	Cambridge	MA	US
Walters, W. Patrick	Westborough	MA	US

US-CL-CURRENT: 703/11

Full | Title | Citation | Front | Review | Classification | Date | Reference | Sequences | Attachments | Claims | KWIC | Draw D

☐ 7. Document ID: US 20040220202 A1

L7: Entry 7 of 12 File: PGPB Nov 4, 2004

PGPUB-DOCUMENT-NUMBER: 20040220202
PGPUB-FILING-TYPE: new
DOCUMENT-IDENTIFIER: US 20040220202 A1

TITLE: Neuroprotective and anti-proliferative compounds

PUBLICATION-DATE: November 4, 2004

INVENTOR-INFORMATION:

NAME	CITY	STATE	COUNTRY
Jaquith, James B.	Pincourt		CA
Fallis, Alexander Graham	Ottawa		CA
Gillard, John W.	Baie D'Urfe		CA
Laurent, Alain	Montreal		CA

US-CL-CURRENT: 514/280; 514/410, 546/41, 548/416

Full | Title | Citation | Front | Review | Classification | Date | Reference | Sequences | Attachments | Claims | KWIC | Draw. D

☐ 8. Document ID: US 20040171075 A1

L7: Entry 8 of 12 File: PGPB Sep 2, 2004

PGPUB-DOCUMENT-NUMBER: 20040171075
PGPUB-FILING-TYPE: new
DOCUMENT-IDENTIFIER: US 20040171075 A1

TITLE: Modulation of protein functionalities

PUBLICATION-DATE: September 2, 2004

INVENTOR-INFORMATION:

NAME	CITY	STATE	COUNTRY
Flynn, Daniel L.	Lawrence	KS	US
Petillo, Peter A.	Arlington	MA	US

US-CL-CURRENT: 435/7.1; 702/19

Full | Title | Citation | Front | Review | Classification | Date | Reference | Sequences | Attachments | Claims | KWIC | Draw. D

☐ 9. Document ID: US 20040102467 A1

L7: Entry 9 of 12 File: PGPB May 27, 2004

PGPUB-DOCUMENT-NUMBER: 20040102467
PGPUB-FILING-TYPE: new
DOCUMENT-IDENTIFIER: US 20040102467 A1

TITLE: Neuroprotective and anti-proliferative compounds

PUBLICATION-DATE: May 27, 2004

INVENTOR-INFORMATION:

NAME	CITY	STATE	COUNTRY
Jaquith, James B	Pincourt		CA
Fallis, Alex	Ottawa		CA
Gillard, John W	Baie D'Urfe		CA

US-CL-CURRENT: 514/279; 514/394, 546/40, 548/305.1

Full | Title | Citation | Front | Review | Classification | Date | Reference | Sequences | Attachments | Claims | KWIC | Draw D

☐ 10. Document ID: US 20040009569 A1

L7: Entry 10 of 12 File: PGPB Jan 15, 2004

PGPUB-DOCUMENT-NUMBER: 20040009569
PGPUB-FILING-TYPE: new
DOCUMENT-IDENTIFIER: US 20040009569 A1

TITLE: Kinase crystal structures and materials and methods for kinase activation

PUBLICATION-DATE: January 15, 2004

INVENTOR-INFORMATION:

NAME	CITY	STATE	COUNTRY
Barford, David	London		GB
Yang, Jing	Middlesex		GB
Hemmings, Brian Arthur	Bettingen		CH
Cron, Peter David	Basel		CH

US-CL-CURRENT: 435/194; 702/19

Full | Title | Citation | Front | Review | Classification | Date | Reference | Sequences | Attachments | Claims | KWIC | Draw D

☐ 11. Document ID: US 20040005687 A1

L7: Entry 11 of 12 File: PGPB Jan 8, 2004

PGPUB-DOCUMENT-NUMBER: 20040005687
PGPUB-FILING-TYPE: new
DOCUMENT-IDENTIFIER: US 20040005687 A1

TITLE: Kinase crystal structures

PUBLICATION-DATE: January 8, 2004

INVENTOR-INFORMATION:

NAME	CITY	STATE	COUNTRY
Barford, David	London		GB
Yang, Jing	Middlesex		GB
Hemmings, Brian Arthur	Bettingen		CH
Cron, Peter David	Basel		CH

US-CL-CURRENT: 435/194; 702/19

Full | Title | Citation | Front | Review | Classification | Date | Reference | Sequences | Attachments | Claims | KWIC | Draw D

☐ 12. Document ID: US 20030194745 A1

L7: Entry 12 of 12 File: PGPB Oct 16, 2003

PGPUB-DOCUMENT-NUMBER: 20030194745
PGPUB-FILING-TYPE: new
DOCUMENT-IDENTIFIER: US 20030194745 A1

TITLE: Cysteine mutants and methods for detecting ligand binding to biological molecules

PUBLICATION-DATE: October 16, 2003

INVENTOR-INFORMATION:

NAME	CITY	STATE	COUNTRY
McDowell, Robert S.	San Francisco	CA	US
Flanagan, W. Michael	Menlo Park	CA	US

US-CL-CURRENT: 435/7.1; 702/19

Full | Title | Citation | Front | Review | Classification | Date | Reference | Sequences | Attachments | Claims | KWIC | Draw D

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Search Results - Record(s) 1 through 17 of 17 returned.

☐ 1. Document ID: US 6890747 B2

Using default format because multiple data bases are involved.

L9: Entry 1 of 17 File: USPT May 10, 2005

US-PAT-NO: 6890747
DOCUMENT-IDENTIFIER: US 6890747 B2

TITLE: Phosphoinositide 3-kinases

DATE-ISSUED: May 10, 2005

INVENTOR-INFORMATION:

NAME	CITY	STATE	ZIP CODE	COUNTRY
Williams; Roger	Cambridge			GB
Ried; Christian	Berlin			DE
Walker; Edward H.	Chesterton			GB
Stephens; Len	Horseheath			GB

US-CL-CURRENT: 435/194

Full | Title | Citation | Front | Review | Classification | Date | Reference | Sequences | Attachments | Claims | KWIC | Draw De

☐ 2. Document ID: US 6780625 B2

L9: Entry 2 of 17 File: USPT Aug 24, 2004

US-PAT-NO: 6780625
DOCUMENT-IDENTIFIER: US 6780625 B2

TITLE: Glycogen synthase kinase-3 inhibitors

DATE-ISSUED: August 24, 2004

INVENTOR-INFORMATION:

NAME	CITY	STATE	ZIP CODE	COUNTRY
Eldar-Finkelman; Hagit	Shoham			IL

US-CL-CURRENT: 435/194; 435/15, 514/7, 530/324, 530/325, 530/326, 530/327, 530/328, 530/329

ABSTRACT:

Peptide inhibitors of glycogen synthase kinase-3 (GSK-3) have an amino acid sequence motif of XZXXXS(p)X, wherein S(p)=phosphorylated serine or phosphorylated threonine, X=any amino acid, and Z=any amino acid except serine or threonine. These inhibitors, which are about 7 to 50 amino acids long, are specific for GSK-3 and strongly inhibit the enzyme with an IC.sub.50 of about 150 .mu.M. Also provided are methods of treating biological conditions mediated by GSK-3 activity, such as potentiating insulin signaling in a subject, treating or preventing type 2 diabetes in a patient, and treating Alzheimer's Disease by administering peptide inhibitors. Compositions of these peptide inhibitors and pharmaceutically acceptable carriers are also provided, as is a method for identifying inhibitors of GSK-3. The invention further relates to a computer-assisted method of structure based drug design of GSK-3 inhibitors using a three-dimensional structure of a peptide substrate of GSK-3.

13 Claims, 11 Drawing figures
Exemplary Claim Number: 1
Number of Drawing Sheets: 7

☐ 3. Document ID: US 5352388 A

L9: Entry 3 of 17 File: USPT Oct 4, 1994

US-PAT-NO: 5352388
DOCUMENT-IDENTIFIER: US 5352388 A

TITLE: Non-linear optical device

DATE-ISSUED: October 4, 1994

INVENTOR-INFORMATION:

NAME	CITY	STATE	ZIP CODE	COUNTRY
Seddon; Kenneth R.	West Sussex			GB2
Aakeroy; Christer B.	West Sussex			GB2
Blagden; Nicholas	Merseyside			GB2
Patell; Yasmin	Kent			GB2

US-CL-CURRENT: 252/582; 252/587, 359/328

ABSTRACT:

A non-linear optical device comprises a crystalline, second harmonic generator material mounted in the optical path of a laser, in which the crystalline material consists of a slat of a chiral carboxylic acid and an organic nitrogenous base which has a noncentrosymmetric crystal structure.

10 Claims, 1 Drawing figures
Exemplary Claim Number: 1
Number of Drawing Sheets: 1

☐ 4. Document ID: WO 3016517 A2

L9: Entry 4 of 17 File: EPAB Feb 27, 2003

PUB-NO: WO003016517A2
DOCUMENT-IDENTIFIER: WO 3016517 A2
TITLE: KINASE CRYSTAL STRUCTURES

PUBN-DATE: February 27, 2003

INVENTOR-INFORMATION:

NAME	COUNTRY
BARFORD, DAVID	GB
YANG, JING	GB
HEMMINGS, BRIAN ARTHUR	CH
CRON, PETER DAVID	CH

INT-CL (IPC): C12 N 9/12; C12 N 15/54; C12 N 5/10; G01 N 33/573; G01 N 23/20
EUR-CL (EPC): C12N009/12

ABSTRACT:

CHG DATE=20030403 STATUS=O>Disclosed are mutants of protein kinase B/Akt which can be crystallised in an enzymaticallyactive conformation, crystals of these mutants and X-ray coordinate data for the crystals.Also disclosed are methods of using the coordinate data provided for identification ofmodulators of protein kinase activity and for structural analysis of other proteinkinases, in particular AGC kinases.

Full | Title | Citation | Front | Review | Classification | Date | Reference | Sequences | Attachments | Claims | KWIC | Draw. D

☐ 5. Document ID: WO 3016516 A2

L9: Entry 5 of 17 File: EPAB Feb 27, 2003

PUB-NO: WO003016516A2
DOCUMENT-IDENTIFIER: WO 3016516 A2
TITLE: KINASE CRYSTAL STRUCTURES AND MATERIALS AND METHODS FOR KINASE ACTIVATION

PUBN-DATE: February 27, 2003

INVENTOR-INFORMATION:

NAME	COUNTRY
BARFORD, DAVID	GB
YANG, JING	GB
HEMMINGS, BRIAN ARTHUR	CH
CRON, PETER DAVID	CH

INT-CL (IPC): C12 N 9/12; C12 N 15/54; C12 N 5/10; G01 N 33/573; G01 N 23/20
EUR-CL (EPC): C12N009/12

ABSTRACT:

CHG DATE=20030403 STATUS=O>Disclosed are crystallisable mutants of protein kinase B/Akt, crystals of these mutants, and X-ray coordinate data for the crystals. Methods of use of the coordinate data for identification of modulators of protein kinase activity and for structural analysis of other protein kinases are provided. Also provided are methods of activating protein kinases, in particular AGC kinases, using peptide or non-peptide mimetics of sequences from protein kinase B/Akt, or other AGC protein kinases such as PRK2.

☐ 6. Document ID: WO 2005113762 A1

L9: Entry 6 of 17 File: DWPI Dec 1, 2005

DERWENT-ACC-NO: 2006-056460
DERWENT-WEEK: 200606

TITLE: New crystal composition of the catalytic domain of the active form of protein kinase B (Akt-1) useful in identifying Akt-1 ligands for treating cancers

INVENTOR: PANDIT, J

PRIORITY-DATA: 2004US-572304P (May 18, 2004)

PATENT-FAMILY:

PUB-NO	PUB-DATE	LANGUAGE	PAGES	MAIN-IPC
WO 2005113762 A1	December 1, 2005	E	142	C12N009/12

INT-CL (IPC): C12 N 9/12

ABSTRACTED-PUB-NO: WO2005113762A
BASIC-ABSTRACT:

NOVELTY - Crystal composition (I) of the catalytic domain of the active form of protein kinase B (Akt-1), is new.

DETAILED DESCRIPTION - INDEPENDENT CLAIMS are also included for:

(1) a crystal (II) of a protein-ligand molecule or molecular complex comprising: a polypeptide with an amino acid sequence from Arg144 to Ala480 listed in a fully defined 480 amino acid (SEQ ID No. 1) sequence given in the specification, its homologue, analogue or variant; a ligand; and the crystal effectively diffracts X-rays for the determination of atomic structure coordinates of the protein-ligand complex to a resolution of greater than 2.02 Angstroms;

(2) designing a compound that binds to Akt-1 using (I), comprising selecting a compound by performing structure-based drug design with the atomic structure

coordinated determined for the crystal, where the selection is performed in conjunction with computer modeling;

(3) a computer for producing a three-dimensional representation of a polypeptide with an amino acid sequence spanning amino acids Arg144 to Ala480 listed in SEQ ID NO. 1, or its homologue or variant, comprising: a computer-readable data storage medium comprising a data storage material encoded with computer-readable data (where the data comprises the structure coordinates that are given in the specification) or its portions; a working memory for storing instructions for processing the computer-readable data; a central-processing unit coupled to the working memory and to the computer-readable data storage medium for processing the computer-machine readable data into the three-dimensional representation; and a display coupled to the central-processing unit for displaying the representation;

(4) a computer for producing a three-dimensional representation of a molecule or molecular complex comprising: a binding site defined by the structure coordinates that are given in the specification, or the structural coordinates of a portion of the residues that are given in the specification, or the structural coordinates of one or more Akt-1 amino acids in SEQ ID NO. 1 (Val164, Ala177, Lys179, Glu228, Tyr229, Ala230, Lys276, Met281 or Thr291), where the computer comprises; a computer-readable data storage medium comprising a data storage material encoded with computer-readable data, where the data comprises the structure coordinates that are given in the specification, or its portions; a working memory for storing instructions for processing the computer-readable data; a central-processing unit coupled to the working memory and to the computer-readable data storage medium for processing the computer machine readable data into the three-dimensional representation; and a display coupled to the central-processing unit for displaying the representation; and

(5) identifying potential ligands for Akt-1 or its homologues, analogues or variants, comprising: displaying three dimensional structure of Akt-1 enzyme or its portions, as defined by atomic structure coordinates given in the specification, on a computer display screen; optionally replacing one or more Akt-1 enzyme amino acid residues listed in SEQ ID NO. 1, or one or more of the amino acids listed in the tables of the specification, or one or more amino acid residues (Val164, Ala177, Lys179, Glu228, Tyr229, Ala230, Lys276, Met281 or Thr291) in the three-dimensional structure with a different naturally occurring amino acid or an unnatural amino acid; employing the three-dimensional structure to design or select the ligand; contacting the ligand with Akt-1 or its variant, in the presence of one or more substrates; and measuring the ability of the ligand to modulate the activity of Akt-1.

ACTIVITY - Cytostatic.

No biological data given.

MECHANISM OF ACTION - None given.

USE - (I) is useful in identifying Akt-1 ligands, including Akt-1 inhibitor compounds; and the compositions containing the ligand are useful for the treatment of a variety of cancers (e.g. breast, prostate, colon, lung pancreas and colorectal cancers).

☐ 7. Document ID: JP 2005525785 W, WO 2003016517 A2, US 20040005687 A1, EP 1417303 A2, AU 2002321458 A1

L9: Entry 7 of 17 File: DWPI Sep 2, 2005

DERWENT-ACC-NO: 2003-268329
DERWENT-WEEK: 200559

TITLE: New crystal of protein kinase B beta, useful for activating protein kinases, e.g. AGC kinases, comprises three-dimensional atomic coordinates or a tetragonal space group

INVENTOR: BARFORD, D; CRON, P D ; HEMMINGS, B A ; YANG, J

PRIORITY-DATA: 2002GB-0016215 (July 12, 2002), 2001GB-0019860 (August 14, 2001), 2002GB-0009985 (May 1, 2002)

PATENT-FAMILY:

PUB-NO	PUB-DATE	LANGUAGE	PAGES	MAIN-IPC
JP 2005525785 W	September 2, 2005		205	C12N009/12
WO 2003016517 A2	February 27, 2003	E	124	C12N009/12
US 20040005687 A1	January 8, 2004		000	G06F019/00
EP 1417303 A2	May 12, 2004	E	000	C12N009/12
AU 2002321458 A1	March 3, 2003		000	C12N009/12

INT-CL (IPC): C07 K 19/00; C12 N 5/10; C12 N 9/12; C12 N 15/54; G01 N 23/20; G01 N 33/48; G01 N 33/50; G01 N 33/573; G06 F 17/30; G06 F 19/00

ABSTRACTED-PUB-NO: WO2003016517A
BASIC-ABSTRACT:

NOVELTY - A crystal of protein kinase B beta (PKB beta) comprising (I), is new. 3-D protein coordinate data is given in the specification.

DETAILED DESCRIPTION - (I) comprises:

(a) a tetragonal space group P212121, and unit cell dimensions of: a = 44.94 plus or minus 0.5 Angstrom , b = 61.00 plus or minus 0.5 Angstrom , c = 131.32 plus or minus 0.5 Angstrom ; or

(b) the three-dimensional atomic coordinates fully defined in the specification.

INDEPENDENT CLAIMS are included for the following:

(1) determining the structure of a PKB derivative;

(2) analyzing a PKB beta -ligand complex;

(3) determining a three-dimensional structure for a target kinase;

(4) a computer system or computer-readable media containing:

(a) atomic coordinate data listed in the specification, which defines the three-dimensional structure of PKB, or at least its selected coordinates;

(b) structure factor data derived from the atomic coordinate data cited above;

(c) a Fourier transform of the atomic coordinate data cited above;

(d) atomic coordinate data of a target kinase generated by homology modeling of the target based on the data listed in the specification;

(e) atomic coordinate data of a target kinase generated by interpreting X-ray crystallographic data or NMR data by reference to any of the data listed in the specification; or

(f) structure factor data derived from the atomic coordinate data of (c)-(e);

(5) modeling the interaction between PKB and an agent compound that modulates PKB activity;

(6) identifying an agent compound that modulates PKB activity; and

(7) a compound identified as a modulator of PKB activity by method (6).

ACTIVITY - Cytostatic; Antidiabetic; Vasotropic; Nootropic; Neuroprotective. No biological data given.

MECHANISM OF ACTION - Gene therapy.

USE - The crystal of PKB beta and methods are useful in activating protein kinases, particularly AGC kinases, for identifying modulators of protein kinase activity, and for structural analysis of other protein kinases. The crystal may also be used in manufacturing a medicament for treating cancers, diabetes, erectile dysfunction or neurodegeneration.

☐ 8. Document ID: JP 2005500844 W, WO 2003016516 A2, US 20040009569 A1, EP 1417302 A2, EP 1417303 A2, AU 2002321457 A1

L9: Entry 8 of 17 File: DWPI Jan 13, 2005

DERWENT-ACC-NO: 2003-268328
DERWENT-WEEK: 200506

TITLE: New crystal of protein kinase B beta, useful for activating protein kinases, e.g. AGC kinases, comprises three-dimensional atomic coordinates or a tetragonal space group

INVENTOR: BARFORD, D; CRON, P D ; HEMMINGS, B A ; YANG, J

PRIORITY-DATA: 2002GB-0009985 (May 1, 2002), 2001GB-0019860 (August 14, 2001), 2002GB-0016215 (July 12, 2002)

PATENT-FAMILY:

PUB-NO	PUB-DATE	LANGUAGE	PAGES	MAIN-IPC
JP 2005500844 W	January 13, 2005		551	C12N015/09
WO 2003016516 A2	February 27, 2003	E	142	C12N009/12
US 20040009569 A1	January 15, 2004		000	G06F019/00
EP 1417302 A2	May 12, 2004	E	000	C12N009/12
EP 1417303 A2	May 12, 2004	E	000	C12N009/12

AU 2002321457 A1 March 3, 2003 000 C12N009/12

INT-CL (IPC): C12 N 1/15; C12 N 1/19; C12 N 1/21; C12 N 5/10; C12 N 9/12; C12 N 15/09; C12 N 15/54; G01 N 23/20; G01 N 33/15; G01 N 33/48; G01 N 33/50; G01 N 33/573; G01 R 33/465; G06 F 19/00

ABSTRACTED-PUB-NO: WO2003016516A
BASIC-ABSTRACT:

NOVELTY - A crystal of protein kinase B beta (PKB beta) comprising (I), is new.

DETAILED DESCRIPTION - (I) comprises:

(a) a tetragonal space group P41212 and unit cell dimensions of: a = 149.33 plus or minus 0.5 Angstrom , b = 149.33 plus or minus 0.5 Angstrom , c = 39.77 plus or minus 0.5 Angstrom ; a = 148.40 plus or minus 0.5 Angstrom , b = 148.40 plus or minus 0.5 Angstrom , c = 38.55 plus or minus 0.5 Angstrom ; a = 149.70 plus or minus 0.5 Angstrom , b = 149.70 plus or minus 0.5 Angstrom , c = 39.19 plus or minus 0.5 Angstrom ; or a = 149.52 plus or minus 0.5 Angstrom , b = 149.52 plus or minus 0.5 Angstrom , c = 39.06 plus or minus 0.5 Angstrom ; or

(b) the three-dimensional atomic coordinates listed in the specification.

INDEPENDENT CLAIMS are also included for:

(1) crystallizing (M1) a PKB derivative;

(2) determining (M2) the structure of a PKB derivative;

(3) a PKB polypeptide having an N-terminus corresponding to Lys-146 of human PKB beta ;

(4) a nucleic acid encoding the polypeptide;

(5) a vector comprising the nucleic acid;

(6) a host cell comprising the nucleic acid or vector;

(7) preparing (M3) a polypeptide;

(8) analyzing (M4) a PKB beta -ligand complex;

(9) determining (M5) a three-dimensional structure for a target kinase, or for determining three-dimensional atomic coordinate data for a target conformation of a PKB isoform;

(10) a computer system or computer-readable media containing:

(a) atomic coordinate data listed in the specification, which defines the three-dimensional structure of PKB, or at least its selected coordinates;

(b) structure factor data derived from the atomic coordinate data;

(c) a Fourier transform of the atomic coordinate data;

(d) atomic coordinate data of a target kinase generated by homology modeling of the target based on the data listed in the specification;

(e) atomic coordinate data of a target kinase generated by interpreting X-ray

crystallographic data or NMR data by reference to any of the data listed in the specification; or

(f) structure factor data derived from the atomic coordinate data of (c)-(e);

(11) modeling (M6) the interaction between PKB and an agent compound that modulates PKB activity;

(12) identifying (M7) an agent compound that modulates PKB activity;

(13) a compound identified as a modulator of PKB activity by M7;

(14) inducing (M8) a catalytic domain of an AGC kinase to adopt an active conformation, where the AGC kinase in its native form is regulated by phosphorylation of a regulatory phosphorylation site residue in a C-terminal regulatory segment distinct from the catalytic domain;

(15) a non-covalent complex between a catalytic domain of the AGC kinase cited above and an activating agent;

(16) determining (M9) the structure of an active conformation of a catalytic domain of the AGC kinase cited above;

(17) assessing (M10) the ability of a candidate compound to modulate the catalytic activity of the AGC kinase; and

(18) a mutant AGC kinase protein comprising a catalytic domain, a C-terminal regulatory segment distinct from the catalytic domain, and an N-terminus corresponding to residue 139-150 of human PKB beta , or their corresponding residues in other isoforms, and a mutation which enhances the interaction between the regulatory segment and the catalytic domain relative to the wild-type enzyme, such that an active conformation is induced in the catalytic domain.

ACTIVITY - Cytostatic; Antidiabetic; Vasotropic; Nootropic; Neuroprotective.

No biological data given.

MECHANISM OF ACTION - Gene therapy.

USE - The crystal of PKB beta and methods are useful in activating protein kinases, particularly AGC kinases, for identifying modulators of protein kinase activity, and for structural analysis of other protein kinases. The crystal may also be used in manufacturing a medicament for treating cancers, diabetes, erectile dysfunction or neurodegeneration.

☐ 9. Document ID: US 3808190 A

L9: Entry 9 of 17 File: USOC Apr 30, 1974

US-PAT-NO: 3808190
DOCUMENT-IDENTIFIER: US 3808190 A

TITLE: PROCESS FOR THE PREPARATION OF ASPARTYL DIPEPTIDE ESTERS INVOLVING LITTLE RACEMIZATION

DATE-ISSUED: April 30, 1974

INVENTOR-NAME: BOESTEN W; DAHLMANS J ; DASSEN B

US-CL-CURRENT: 560/40, 530/801, 548/497, 548/533, 560/125, 560/153, 560/163, 560/168, 560/169, 560/39, 560/41CIPG20060101AA23LA23L1

Full | Title | Citation | Front | Review | Classification | Date | Reference | Sequences | Attachments | Claims | KWIC | Draw D

☐ 10. Document ID: US 3772315 A

L9: Entry 10 of 17 File: USOC Nov 13, 1973

US-PAT-NO: 3772315
DOCUMENT-IDENTIFIER: US 3772315 A

TITLE: PROCESS FOR THE PRODUCTION OF 2-ACYLIMIDAZOLES

DATE-ISSUED: November 13, 1973

INVENTOR-NAME: REGEL E; BUCHEL K

US-CL-CURRENT: 546/274.7, 548/127, 548/233, 548/236, 548/243, 548/244, 548/245, 548/246, 548/247, 548/304.7, 548/306.1, 548/309.4, 548/312.4, 548/315.1, 548/315.4, 548/333.5, 548/335.1CIPG20060101AC07DC07D233

Full | Title | Citation | Front | Review | Classification | Date | Reference | Sequences | Attachments | Claims | KWIC | Draw D

☐ 11. Document ID: US 3732232 A

L9: Entry 11 of 17 File: USOC May 8, 1973

US-PAT-NO: 3732232
DOCUMENT-IDENTIFIER: US 3732232 A

TITLE: PROCESS FOR THE PREPARATION OF IMIDAZOISOQUINOLINEDIONE COMPOUNDS

DATE-ISSUED: May 8, 1973

INVENTOR-NAME: EUE L; REGEL E ; BUCHEL K

US-CL-CURRENT: 546/84, 504/245, 548/304.4, 548/335.1, 548/343.1, 548/343.5CIPG20060101AC07DC07D471

Full | Title | Citation | Front | Review | Classification | Date | Reference | Sequences | Attachments | Claims | KWIC | Draw D

☐ 12. Document ID: US 3632843 A

L9: Entry 12 of 17 File: USOC Jan 4, 1972

US-PAT-NO: 3632843

DOCUMENT-IDENTIFIER: US 3632843 A

TITLE: BIS(PERFLUOROALKYLSULFONYL)METHANES IN CATIONIC POLYMERIZATION

DATE-ISSUED: January 4, 1972

INVENTOR-NAME: BEEBE GEORGE W; ALLEN MICHAEL GEORGE

US-CL-CURRENT: 528/45, 502/168, 525/524, 526/217, 526/225, 526/234, 528/10, 528/109, 528/129, 528/26, 528/28, 528/364, 528/373, 528/408, 528/73, 528/90CIPG20060101AC08FC08F4

Full | Title | Citation | Front | Review | Classification | Date | Reference | Sequences | Attachments | Claims | KWIC | Draw D

☐ 13. Document ID: US 3427315 A

L9: Entry 13 of 17 File: USOC Feb 11, 1969

US-PAT-NO: 3427315
DOCUMENT-IDENTIFIER: US 3427315 A

TITLE: PROCESS FOR PREPARING PURINE DERIVATIVES

DATE-ISSUED: February 11, 1969

INVENTOR-NAME: NOMURA HIROAKI; UNO NORIHIRO ; SUGIMOTO KEIICHI

US-CL-CURRENT: 544/265, 544/277

Full | Title | Citation | Front | Review | Classification | Date | Reference | Sequences | Attachments | Claims | KWIC | Draw D

☐ 14. Document ID: US 3420827 A

L9: Entry 14 of 17 File: USOC Jan 7, 1969

US-PAT-NO: 3420827
DOCUMENT-IDENTIFIER: US 3420827 A

TITLE: PROCESS FOR MAKING 4,4-DIMETHYL-3-BUTENYL METHYL KETONES,INTERMEDIATES THEREFOR AND THE SAID INTERMEDIATES

DATE-ISSUED: January 7, 1969

INVENTOR-NAME: LEFFINGWELL JOHN C

US-CL-CURRENT: 544/171; 544/106, 548/573, 560/168, 560/170, 560/172, 568/398, 568/417

Full | Title | Citation | Front | Review | Classification | Date | Reference | Sequences | Attachments | Claims | KWIC | Draw D

☐ 15. Document ID: US 3367910 A

L9: Entry 15 of 17 File: USOC Feb 6, 1968

US-PAT-NO: 3367910
DOCUMENT-IDENTIFIER: US 3367910 A

TITLE: Modihed organopolysiloxanes and method of preparation

DATE-ISSUED: February 6, 1968

INVENTOR-NAME: NEWING JR CHARLES W

US-CL-CURRENT: 528/19; 252/301.35, 273/DIG.29, 524/175, 524/176, 524/779, 528/20, 528/32, 528/43

Full | Title | Citation | Front | Review | Classification | Date | Reference | Sequences | Attachments | Claims | KWIC | Draw D

☐ 16. Document ID: US 3193533 A

L9: Entry 16 of 17 File: USOC Jul 6, 1965

US-PAT-NO: 3193533
DOCUMENT-IDENTIFIER: US 3193533 A

TITLE: Polymerization of formaldehyde

DATE-ISSUED: July 6, 1965

INVENTOR-NAME: HARDING MANWILLER CARL; BROCKWAY THOMPSON JOHN

US-CL-CURRENT: 528/239, 528/232

Full | Title | Citation | Front | Review | Classification | Date | Reference | Sequences | Attachments | Claims | KWIC | Draw D

☐ 17. Document ID: US 2747988 A

L9: Entry 17 of 17 File: USOC May 29, 1956

US-PAT-NO: 2747988
DOCUMENT-IDENTIFIER: US 2747988 A

TITLE: Method for the recovery of pure iron oxide and iron from oxidic iron ores

DATE-ISSUED: May 29, 1956

INVENTOR-NAME: VON HAKEN KURD

US-CL-CURRENT: 75/10.67; 266/137, 266/163, 266/177, 420/88, 75/10.44, 75/10.58, 75/481, 75/503

Full | Title | Citation | Front | Review | Classification | Date | Reference | Sequences | Attachments | Claims | KWIC | Draw. De

Clear | Generate Collection | Print | Fwd Refs | Bkwd Refs | Generate OACS

Terms	Documents
L8 same crystal	17

Display Format: - Change Format

Previous Page Next Page Go to Doc#

FILE 'HOME' ENTERED AT 17:58:14 ON 05 APR 2006

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=> s akt3 or protein kinase b γ or pkbγ
L1          85 FILE MEDLINE
L2         155 FILE CAPLUS
L3          80 FILE SCISEARCH
L4          26 FILE LIFESCI
L5          92 FILE BIOSIS
L6          64 FILE EMBASE

TOTAL FOR ALL FILES
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=> d ibib abs

L29  ANSWER 1 OF 4  CAPLUS  COPYRIGHT 2006 ACS on STN
ACCESSION NUMBER:         2006:193616  CAPLUS Full-text
DOCUMENT NUMBER:          144:249421
TITLE:                    Crystal structures of Akt3 kinase
                          and its mutants and complexes with thiophene
                          inhibitors and methods for molecular modeling in drug
                          design
INVENTOR(S):              Bussiere, Dirksen; Fang, Eric; Murray, Jeremy
PATENT ASSIGNEE(S):       Chiron Corporation, USA
SOURCE:                   PCT Int. Appl., 228 pp.
                          CODEN: PIXXD2
DOCUMENT TYPE:            Patent
LANGUAGE:                 English
FAMILY ACC. NUM. COUNT:   1
PATENT INFORMATION:

     PATENT NO.           KIND   DATE        APPLICATION NO.        DATE
     ---------------      ----   --------    -------------------    --------
     WO 2006022718         A1    20060302    WO 2004-US26569        20040813
         W:  AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BW, BY, BZ, CA, CH,
             CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD,
             GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC,
             LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NA, NI,
             NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SY,
             TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW
         RW: AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE,
             IT, LU, MC, NL, PL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI,
             CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG, BW, GH, GM, KE, LS,
             MW, MZ, NA, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD,
             RU, TJ, TM
PRIORITY APPLN. INFO.:                       WO 2004-US26569        20040813
```

AB The atomic coordinates of human Akt3 kinase residues 138-479 and its double mutant T305D/S472D, alone and in complexes with the inhibitors N-[(1S)-2-amino-1-(2,4-dichlorobenzyl)ethyl]-5-[2-(methylamino)pyrimidin-4- yl]thiophene-2-carboxamide or N-[6(aminomethyl)-4-chloro-1,3-benzothiazol- 2-yl]-5-(2-aminopyrimidin-4-yl)thiophene-2-carboxamide, were determined by x-ray crystallog. The present invention relates 3-dimensional structure of Akt3 and its mutants, methods for crystallization and the crystals, and to methods for using mol. modeling to design and identify therapeutic compds. for the treatment of Akt3-mediated diseases.

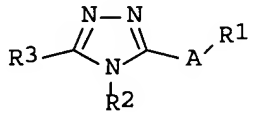
REFERENCE COUNT: 2 THERE ARE 2 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

=> d 2-3 ibib abs

L29 ANSWER 2 OF 4 CAPLUS COPYRIGHT 2006 ACS on STN
ACCESSION NUMBER: 2005:1126670 CAPLUS Full-text
DOCUMENT NUMBER: 143:405912
TITLE: Preparation of triazole-based compounds, particularly thiotriazoles, exhibiting ATP-utilizing enzyme inhibitory activity, and compositions, and uses thereof
INVENTOR(S): Hodge, Carl Nicholas; Dickson, John K., Jr.; Popa-Burke, Ioana G.; Mendoza, Jose Serafin
PATENT ASSIGNEE(S): Amphora Discovery Corporation, USA
SOURCE: PCT Int. Appl., 185 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.		DATE
WO 2005097758	A1	20051020	WO 2005-US10083		20050325
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BW, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NA, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SM, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW					
RW: BW, GH, GM, KE, LS, MW, MZ, NA, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IS, IT, LT, LU, MC, NL, PL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG					
US 2005288347	A1	20051229	US 2005-90956		20050325
PRIORITY APPLN. INFO.:			US 2004-556795P	P	20040326
			US 2004-638944P	P	20041223

OTHER SOURCE(S): MARPAT 143:405912
GI



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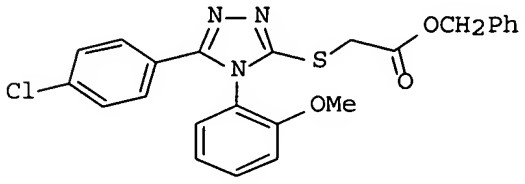

II

AB Preparation of triazoles I [A = S, O, NH and derivs.; R1 = -(CR4R5)n-Q; n = 0-8; R4, R5 = independently H, OH, (un)substituted alkyl; Q = H, S, alkoxy, CO2H and derivs., CN, etc.; R2 = H, (un)substituted alk(en)yl, hetero/aryl, etc.; R3 = H, (un)substituted cyclo/alkyl, hetero/aryl, etc.; with provisos], especially thiotriazole-based compds., and their pharmaceutically acceptable salts, solvates, crystal forms, chelates, non-covalent complexes, and prodrugs exhibiting ATP-utilizing enzyme inhibitory activity (no data), methods of using them, and compns. containing them are described. For example,

thiotriazole II was prepared by reacting 4-chlorobenzhydrazide with 2-methoxyphenyl isothiocyanate, cyclization in the presence of NaOH, and alkylation with benzyl 2-bromoacetate (no isolation of the intermediates). I displayed selective activity for one of the following protein kinases or pair of protein kinases: AKT1, CDK2/cyclin A, DAPK1, ABL1, etc. (no data). I are useful for the treatment of at least one of the diseases selected from Alzheimer's disease, stroke, diabetes, obesity, inflammation, and cancer (no data).

REFERENCE COUNT: 4 THERE ARE 4 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L29 ANSWER 3 OF 4 SCISEARCH COPYRIGHT (c) 2006 The Thomson Corporation on STN

ACCESSION NUMBER: 2005:138403 SCISEARCH Full-text
THE GENUINE ARTICLE: 892PM
TITLE: Identification and characterization of pleckstrin-homology-domain-dependent and isoenzyme-specific Akt inhibitors
AUTHOR: Barnett S F (Reprint); Defeo-Jones D; Fu S; Hancock P J; Haskell K M; Jones R E; Kahana J A; Kral A M; Leander K; Lee L L; Malinowski J; McAvoy E M; Nahas D D; Robinson R G; Huber H E
CORPORATE SOURCE: Merck & Co Inc, Dept Canc Res, W Point, PA 19454 USA (Reprint); Merck & Co Inc, Dept Biol Chem, W Point, PA 19454 USA; Merck & Co Inc, Dept Bioproc Engn, W Point, PA 19454 USA
stan_barnett@merck.com
COUNTRY OF AUTHOR: USA
SOURCE: BIOCHEMICAL JOURNAL, (15 JAN 2005) Vol. 385, Part 2, pp. 399-408.
ISSN: 0264-6021.
PUBLISHER: PORTLAND PRESS LTD, 59 PORTLAND PLACE, LONDON W1B 1QW, ENGLAND.
DOCUMENT TYPE: Article; Journal
LANGUAGE: English
REFERENCE COUNT: 53
ENTRY DATE: Entered STN: 18 Feb 2005
Last Updated on STN: 18 Feb 2005
ABSTRACT IS AVAILABLE IN THE ALL AND IALL FORMATS

AB We developed a high-throughput HTRF (homogeneous time-resolved fluorescence) assay for Akt kinase activity and screened approx. 270000 compounds for their ability to inhibit the three isoforms of Akt. Two Akt inhibitors were identified that exhibited isoenzyme specificity. The first compound (Akt-I-1) inhibited only Akt1 (IC50 4.6muM) while the second compound (Akt-I-1,2) inhibited both Akt1 and Akt2 With IC50 values of 2.7 and 21 muM respectively. Neither compound inhibited Akt3 nor mutants lacking the PH (pleckstrin homology) domain at concentrations up to 250 muM. These compounds were reversible inhibitors, and exhibited a linear mixed-type inhibition against ATP and peptide substrate. In addition to inhibiting kinase activity of individual Akt isoforms, both inhibitors blocked the phosphorylation and activation of the corresponding Akt isoforms by PDK1 (phosphoinositide-dependent kinase 1). A model is proposed in which these inhibitors bind to a site formed only in the presence of the PH domain. Binding of the inhibitor is postulated to promote the formation of an inactive, conformation. In support of this model, antibodies to the Akt PH domain or hinge region blocked the inhibition of Akt by Akt-I-1 and Akt-I-1,2. These inhibitors were found to be cell-active and. to block phosphorylation of Akt at Thr(308) and Ser(473), reduce the levels of active Akt in cells, block the phosphorylation of known Akt substrates and promote TRAIL (tumour-necrosis-factor-related apoptosis-inducing ligand)-induced apoptosis in LNCap prostate cancer cells.

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AB The AKT1, AKT2, and AKT3 kinases have emerged as critical mediators of signal transduction pathways downstream of activated tyrosine kinases and phosphatidylinositol 3-kinase. An ever-increasing list of AKT substrates has precisely defined the multiple functions of this kinase family in normal physiology and disease states. Cellular processes regulated by AKT include cell proliferation and survival, cell size and response to nutrient availability, intermediary metabolism, angiogenesis, and tissue invasion. All these processes represent hallmarks of cancer, and a burgeoning literature has defined the importance of AKT alterations in human cancer and experimental models of tumorigenesis, continuing the legacy represented by the original identification of v-Akt as the transforming oncogene of a murine retrovirus. Many oncoproteins and tumor suppressors intersect in the AKT pathway, finely regulating cellular functions at the interface of signal transduction and classical metabolic regulation. This careful balance is altered in human cancer by a variety of activating and inactivating mechanisms that target both AKT and interrelated proteins. Reprogramming of this altered circuitry by pharmacologic modulation of the AKT pathway represents a powerful strategy for rational cancer therapy. In this review, we summarize a large body of data, from many types of cancer, indicating that AKT activation is one of the most common molecular alterations in human malignancy. We also review mechanisms of activation of AKT kinases, examples of therapeutic modulation of the AKT pathway in animal models, and the current status of efforts to target molecular components of the AKT pathway for cancer therapy and, possibly, cancer prevention.

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